LETTERS TO THE EDITOR

The Role of Arterial Baroreceptors in Mediating the Cardiovascular Response to a Cardiac Glycoside in Conscious Dogs

The study of McRitchie and Vatner (Circ. Res. 38: 321, 1976) raises some questions regarding a possible important effect of ouabain to sensitize baroreceptors. Based on their data, they concluded that “cardiac glycosides do not exert a major action in sensitizing the arterial baroreceptors.” They base their viewpoint on data obtained with ouabain administered to animals with and without sectioned carotid sinus and aortic nerves, and also on comparable data obtained with methoxamine. The pressor effect of both these agents was enhanced threefold by denervating the reflexes. They reasoned that if sensitization of baroreceptors was important in the response to ouabain “a greater difference in arterial pressure response should have been observed in response to ouabain than to methoxamine, because methoxamine is not known to exert a direct effect on the arterial baroreceptors.” This is in contrast with our previous results in decerebrate unanesthetized cats wherein animals with cardiovascular reflexes denervated exhibited a greater difference in arterial pressure response to ouabain than to norepinephrine (Gillis et al., J. Pharmacol. Exp. Ther. 170: 294, 1969). One difference between our experiments and those described in the present study is that, in addition to carotid sinus and aortic arch nerves being sectioned, afferent vagal nerves were also sectioned in our study. This was done because digitalis had been shown to have important actions on cardiac sensory receptors (Kido, Kyushu J. Med. Sci. 3: 149, 1952; Mcville, J. Pharmacol. Exp. Ther. 106: 208, 1952). Indeed, more recent data have indicated an important role of cardiac sensory receptors (via afferent vagal fibers) in the actions of digitalis (Sleigh et al., Circ. Res. 25: 705, 1969; Oberg and Thoren, Acta Physiol. Scand. 85: 145, 1972; Gillis et al., J. Pharmacol. Exp. Ther. 193: 336, 1975). In our study (J. Pharmacol. Exp. Ther. 193: 336, 1975) we found that three reflex regions, namely, carotid sinus, aortic, and cardiac sensory receptors, are involved in digitalis action. Most importantly, we found that the presence of just one of these areas can assume the function of the denervated ones. Thus, it seems to us that McRitchie and Vatner cannot conclude that digitalis does not exert an important effect in sensitizing the baroreceptors unless they perform their experiments in animals with cardiac sensory receptors denervated.

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REPLY TO THE ABOVE LETTER

Dr. Gillis and co-workers have shown that cardiac glycosides sensitize arterial baroreceptors in anesthetized animal preparations.1-3 In a recent article published in Circulation Research4 we observed in conscious animals that arterial baroreceptor deafferentation abolished the bradycardia normally induced by ouabain and induced a threefold greater pressor response, i.e., ouabain increased mean arterial pressure by 11 ± 1 mm Hg in intact dogs and by 33 ± 4 mm Hg in dogs with section of arterial baroreceptor nerves. We felt that if the baroreceptors were sensitized by cardiac glycosides to a degree not exerted by other drugs which increase arterial pressure, then the cardiac glycoside would induce a relatively greater pressor response after arterial baroreceptor deafferentation than methoxamine. Accordingly, we administered an equipressor dose of methoxamine to intact dogs and those with section of arterial baroreceptors. In intact dogs methoxamine increased mean arterial pressure by 10 ± 1 mm Hg and after denervation by 35 ± 3 mm Hg, a response almost identical to that observed for ouabain. With this in mind, we concluded that in the conscious animal ouabain does not exert a major action in sensitizing baroreceptors.4

However, Gillis and co-workers point out that vagal afferents must also be considered,5 and feel that our conclusion is incorrect unless experiments are also performed in animals with cardiac receptors denervated. Accordingly, we have also compared the effects of the same doses of methoxamine and ouabain in conscious dogs with section of arterial baroreceptors and both vagi. Under these circumstances, mean arterial pressure rose by 49 ± 5 mm Hg following ouabain and 57 ± 7 mm Hg following methoxamine. If anything, methoxamine, in comparison with ouabain, caused a greater increase in pressure following vagotomy, further suggesting that ouabain does not have a major baroreceptor-sensitizing action in the conscious animal.

We would suggest that this is one more instance where the circulation of the conscious animal behaves differently from that of the anesthetized animal in response to cardiac glycosides.6-8 Under the conditions of the experiments described by Gillis and co-workers,1-3 where extensive surgical procedures have been carried out under general anesthesia, myocardial contractility must have been depressed considerably. It is, therefore, not surprising that the cardiac glycosides would exert a profound effect on the circulation,
which might not truly reflect its action in the conscious animal, where cardiac depression was not a factor.

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