CHAPTER 3

Large Coronary Artery Regulation by α- and β-Adrenergic Receptors in Conscious Calves

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Summary. Regulation of coronary arteries by α- and β-adrenergic receptor subtype mechanisms was examined in chronically-instrumented, conscious calves. The physiological data on α- and β-adrenergic receptors were correlated with ligand binding studies from sarcolemmal membranes of calf large coronary arteries. In the conscious animal, selective α₁- + α₂- and β₁- + β₂-adrenergic agonists were examined in the presence and absence of selective α₁- + α₂- and β₁- + β₂-adrenergic receptor blockades. Both the α₁-adrenergic agonist, phenylephrine, and the α₂-adrenergic agonist, B-HT 920, induced similar vasoconstriction of the large coronary arteries in the conscious calf, whereas the β₁-adrenergic agonist, prenalterol, and β₂-adrenergic agonist, pirbuterol, induced vasodilation. These effects were abolished by their respective adrenergic subtype blocker, but were not significantly affected by the corresponding blocker for the other subtype. Ligand binding studies demonstrated the presence of both subtypes of α- and β-adrenergic receptors, with a predominance of the β₁- and α₂-adrenergic receptor subtypes. Thus, large coronary arteries of the calf contain both α₁- + α₂- and β₁- + β₂-adrenergic receptor subtypes, and agonists are capable of eliciting significant constriction with either of the α-adrenergic subtypes, and dilation with either of the β-adrenergic subtypes.

Key Words: Ligand binding – Coronary artery diameter – Sympathetic nervous system – Acetylcholine – Adrenergic receptor

Introduction

The regulation of large coronary arteries by α and β-adrenergic receptor subtypes remains controversial [1–5]. Most earlier work has been conducted on isolated preparations due to the difficulties in studying large coronary arteries in the intact animal. The results of previous in vitro studies have suggested that large coronary arteries contain predominantly α₁-adrenergic [6–11] and β₁-
adrenergic [12–17] receptor subtypes, and consequently do not respond to α₂- or β₂-adrenergic stimulation. However, techniques have been developed, which permit the investigation of large coronary artery regulation in the intact, conscious animal [18–22]. These techniques, coupled with ligand binding analyses of adrenergic receptor subtypes, provide a novel approach to reconciling the controversy in this field. The goal of this article is to review the work conducted on the regulation of large coronary arteries in calves, which correlated physiological studies in intact, conscious calves, with ligand binding experiments examining receptor subtype composition in membrane preparations from bovine coronary arteries [18,22].

Materials and Methods

Physiological Studies [18,22]

Female calves, 6–10 weeks old, fully weaned, and weighing 60–80 kg, were anesthetized with halothane (0.5–1.5 vol% in oxygen) following pre-anesthesia with sodium thiamylal (10–15 mg/kg i.v.). Using sterile surgical technique, and with ventilation controlled by a Harvard respirator, a left thoracotomy was performed via the fourth intercostal space. Two miniature ultrasonic dimension transducers were implanted using 5-0 suture on opposing adventitial surfaces of the left circumflex coronary artery, 4–6 cm from its origin. A Doppler blood flow transducer and hydraulic constrictor were implanted in the same vessel. Care was taken during the implantation to avoid excessive dissection and possible damage to the vessel and perivascular nerves. Proximal to the dimension transducers, a silastic catheter was implanted in the left circumflex coronary artery. In addition, Tygon catheters were implanted in the descending aorta and left atrium. Animals used in this study were maintained in accordance with the guidelines of the Committee on Animals of the Harvard Medical School [23] and the National Institutes of Health’s “Guide for Care and Use of Laboratory Animals” [24].

The experiments were conducted 1–3 weeks after surgery in healthy, conscious calves, lying quietly in a cart. Measurements of left circumflex coronary arterial diameter and aortic pressure were continuously recorded. Dose-response relationships to intracoronary selective α₁-adrenergic stimulation with B-HT 920 were examined in the presence of β-adrenergic receptor blockade with propranolol [25–29]. Dose-response relationships to intracoronary selective β₂-adrenergic stimulation with pirbuterol, and selective β₁-adrenergic stimulation with prenalterol were also examined [30–32,18,20–22]. On separate days, the effects of the α-adrenergic agonists were studied following selective α₁-adrenergic receptor blockade with prazosin, and α₂-adrenergic receptor blockade with rauwolscine, and the effects of β-adrenergic agonists were studied following selective β₁-adrenergic receptor blockade with atenolol or betaxolol, and following selective β₂-adrenergic blockade with ICI 118, 551 [18,22]. The data were analyzed using a paired t-test and Bonferroni correction [33].