Discrepant uptake of the radiolabeled norepinephrine analogues hydroxyephedrine (HED) and metaiodobenzylguanidine (MIBG) in rat hearts.

Abstract:
(11)C-Hydroxyephedrine (HED) and radioiodinated metaiodobenzylguanidine ((123)I/(131)I-MIBG) are catecholamine analogue tracers for sympathetic nerve positron emission tomography/single photon emission computed tomography (PET/SPECT) imaging. In contrast to humans, rat hearts demonstrate high nonneural catecholamine uptake-2 in addition to neural uptake-1, the contributions of which to tracer accumulation are not fully elucidated. Wistar rats were studied using the following pretreatments: uptake-1 blockade with desipramine 2 mg/kg IV, both uptake-1 and -2 blockade with phenoxybenzamine 50 mg/kg IV, or control with saline IV. HED or (123)I-MIBG was injected 10 min after pretreatment, and rats were sacrificed 10 min later. Heart to blood tissue count ratio (H/B ratio) was obtained using a gamma counter. To determine regional tracer uptake, dual-tracer autoradiography was performed with HED and (131)I-MIBG in Wistar rats with chronic infarction by transient coronary occlusion and reperfusion and in healthy control rats. Local tracer distributions were analyzed, and the infarcted rats’ local tracer distributions were compared with histology. The H/B ratios in control hearts were 34.4 ± 1.7 and 25.5 ± 2.1 for HED and (123)I-MIBG, respectively. Desipramine led to a
significant decrease in HED (3.2 ± 0.5, p< 0.0001), while there was no change in (123)I-MIBG (25.5 ± 6.4, p = n.s.). Phenoxybenzamine led to a significant decrease in both HED and (123)I-MIBG (3.5 ± 0.02, 4.3 ± 0.7, p< 0.0001). Only HED showed a subepicardium-subendocardium gradient in healthy control hearts which is consistent with physiological innervation, while (131)I-MIBG was evenly distributed throughout the myocardium. (131)I-MIBG uptake defect closely matched the scar area determined by histology [3.8 ± 2.3% ((131)I-MIBG defect) vs 4.0 ± 2.4% (scar)]. However, the scar area was clearly exceeded by the HED uptake defect (9.1 ± 2.2%, p< 0.001).HED uptake showed high specificity to neural uptake-1 in rat hearts. On the other hand, (123)I/(131)I-MIBG demonstrated distinct characters of regional tracer distribution and uptake mechanism that are compatible with significant contribution of nonneural uptake-2.