ORIGINAL ARTICLE

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Cilnidipine as an agent to lower blood pressure without sympathetic nervous activation as demonstrated by iodine-123 metaiodobenzylguanidine imaging in rat hearts

Takatoshi SAKAKI,* Hitoshi NARUSE,* Miho MASAI,* Keiko TAKAHASHI,* Mitsumasa OHYANAGI,* Tadaaki IWASAKI* and Minoru FUKUCHI**

**Department of Internal Medicine, Cardiovascular Division, Hyogo College of Medicine*
***Department of Internal Medicine, Hyogo College of Medicine*

Background: Administration of short-acting antihypertensive agents to patients with ischemic heart disease results in increased sympathetic nervous activity and is associated with worsened outcomes. Cilnidipine is an agent which blocks not only L-type calcium channels at the smooth muscle in the artery, but also N-type calcium channels at the presynaptic terminal. The goal of the present study was to determine the effect of cilnidipine on sympathetic nervous activity as on agent which blocks both L-type and N-type calcium channels at the presynaptic terminal, on sympathetic nervous activity in an experimental rat model using iodine-123 metaiodobenzylguanidine (MIBG) myocardial imaging. ***Methods:*** Fourteen-week-old Wistar-Kyoto rats were divided into 3 separate groups: CTR group (control: distilled water administered), Nif group (nifedipine administered), or Cil group (cilnidipine administered). Agents were administered via a stomach tube, followed by injection of MIBG via the femoral vein. Systolic blood pressure (SBP) and heart rate (HR) were measured by tail-cuff plethysmography just prior to administration of antihypertensive drugs and 150 minutes later. Initial imaging (Ce) and delayed imaging (Cd) were defined as the sum of density counts in the region of interest created by adjusting to myocardial edge, and were corrected for both physical decay and weight. The myocardial washout rate (WR) was defined as the percent change in the count density from the initial to delayed images. ***Results:*** Significant decreases in SBP were seen in the Nif group (from 132 ± 3 mmHg to 85 ± 5 mmHg, $p < 0.0001$) and the Cil group (from 128 ± 4 mmHg to 92 ± 7 mmHg, $p = 0.0008$), whereas no significant change in SBP was noted in the CTR group (from 123 ± 5 mmHg to 127 ± 3 mmHg). HR significantly increased in the Nif group (from 290 ± 12/min to 378 ± 14/min, $p < 0.0001$) but not in the CTR (from 278 ± 3/min to 300 ± 6/min) or Cil (from 291 ± 6/min to 303 ± 5/min) groups. WR was significantly greater in the Nif group ($64.7 \pm 0.5\%$) when compared to the CTR ($56.4 \pm 1.2\%$, $p = 0.0031$) or the Cil ($55.4 \pm 2.2\%$, $p = 0.0016$) groups. ***Conclusion:*** In contrast to nifedipine, administration of cilnidipine did not result in increased myocardial sympathetic nervous activation.

Key words: MIBG, washout rate, N-type Ca channel blocker, myocardial sympathetic nervous activation