Acute carotid sinus stimulation in uncontrolled hypertensive patients

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Extended electric stimulation of the carotid baroreceptors through its modulatory effect on afferent signaling is an attractive target for the treatment of uncontrolled hypertension. Baroreflex sensitivity is usually distressed in hypertension and be unsuccessful to keep blood pressure (BP) at proper levels through its fast-negative feedback loop, in which a raised BP reflexively origins the heart rate to fall and BP to drop. In an initial proof-of-concept study, BAT has been found to exert considerable BP-lowering properties using the CVRx Rheos System (CVRx, Minneapolis, MN) (DEBuT-HT [Device Based Therapy in Hypertension Trial]) comprising implantable electrodes connected to a subcutaneously placed stimulator [1,2]. Implantation of the first-generation device was related to serious procedure-related adverse events, and the short-term battery life restricted its utility. Next-generation devices could essentially overcome these issues and implantation of the Barostim neo (CVRx) was associated with a significant BP decline at 3 and 6 months of follow-up [3]. A recent study in 28 patients [4] exposed further evidence of the positive effects reached by BAT in patients who continued hypertensive despite renal sympathetic denervation performed 5 months earlier. While the BAT device is typically initiated 2 to 4 weeks after surgical implantation to permit the site to heal, immediate activation of BAT in this specific situation created a quick, significant, and sustained reduction in BP. Even though a device that needs surgical placement of electrodes maybe impractical in an emergency condition, the concept of electrical stimulation of the baroreceptors as a means of accomplishing speedy and sustained BP reduction is fascinating and highlights the prospective of this methodology. Further enhancement of the technology and longer-term follow-up of treated patients will support to delineate the clinical value of BAT as an alternative treatment for resistant hypertension.

The well-recognized association between augmented baroreceptors response and parasympathetic activation as an important contributor to the pathophysiology of hypertension led to the initiation of studies investigating the feasibility of a therapeutic intervention aimed at selectively targeting arterial baroreceptors located in the carotid sinus. This transversal study involved 18 uncontrolled hypertensive patients, complaining of pre-syncpe. The study was piloted in agreement with the Helsinki declaration and approved by the ethics committee of our institution. All patients signed the informed consent term connected to a subcutaneously placed stimulator [1,2]. Implantation of the Barostim neo (CVRx) was associated with a significant BP decline at 3 and 6 months of follow-up [3]. A recent study in 28 patients [4] exposed further evidence of the positive effects reached by BAT in patients who continued hypertensive despite renal sympathetic denervation performed 5 months earlier. While the BAT device is typically initiated 2 to 4 weeks after surgical implantation to permit the site to heal, immediate activation of BAT in this specific situation created a quick, significant, and sustained reduction in BP. Even though a device that needs surgical placement of electrodes maybe impractical in an emergency condition, the concept of electrical stimulation of the baroreceptors as a means of accomplishing speedy and sustained BP reduction is fascinating and highlights the prospective of this methodology. Further enhancement of the technology and longer-term follow-up of treated patients will support to delineate the clinical value of BAT as an alternative treatment for resistant hypertension.

The 18 subjects underwent EPS. The primary goal of this study evaluated if carotid sinus stimulation (CSS) can provoke changes in the BP and HR leading to low output symptoms. The procedures were performed in the catheterization laboratory with direct visualization using fluoroscopy and radiopaque contrast. The patients were pretreated with diazepam or midazolam under the supervision of an anesthesiologist. At the end of standard EPS perform, a femoral artery was punctured and a short 6F sheath (St. Jude Medical, St. Paul, Minnesota, USA) was placed into this vessel, allowing introduce and position the quadrupolar dirigible Livewire™ catheter (St. Jude Medical, St. Paul, Minnesota, USA) with a tip electrode of 2 mm, and other electrodes of 1 mm, alternately into the carotid arteries, as close as possible to the carotid sinus on both sides, under fluoroscopic guidance. Unipolar stimulation was performed from the tip of the catheter to target the carotid sinus. The cycle length was set at 200 ms (300 ppm),

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Received: November 01, 2016; Accepted: November 09, 2016; Published: November 14, 2016
Kiuchi MG (2016) Acute carotid sinus stimulation in uncontrolled hypertensive patients

The general features of both groups of patients are listed in Table 1. According to Figure 1A, the right CSS provoked a decrease in the systolic BP from 162.9 ± 9.1 mmHg at baseline to 129.6 ± 5.9 mmHg during stimulation (P<0.0001) and the diastolic BP reduced from 111.4 ± 9.7 to 82.9 ± 3.9 mmHg (P<0.0001), as shown in Figure 1A. The left CSS led to a decrease from 162.4 ± 8.0 mmHg at baseline to 150.5 ± 10.9 mmHg during stimulation (P<0.0001) and the diastolic BP reduced from 110.6 ± 10.0 to 86.0 ± 4.2 mmHg (P<0.0001), as shown in Figure 1B. The comparisons between the variation (∆) of the systolic BP between the right CSS (-33.3 ± 6.4 mmHg) and left CSS (-11.9 ± 6.1 mmHg) was significant (P<0.0001). However, the same comparisons between the ∆ of the diastolic BP between the right CSS (-28.4 ± 9.2 mmHg) and left CSS (-24.6 ± 11.3 mmHg) were not different (P=0.2703), as observed in Figure 1C. The right CSS provoked a decrease at HR from 81.7 ± 6.9 bpm at baseline to 56.2 ± 5.4 bpm (Figure 2A) during stimulation (P<0.0001), and the left CSS provoked a reduction at HR from 82.1 ± 7.1 to 69.4 ± 6.3 bpm (Figure 2B). The comparison between the ∆ of the HR between the right CSS (-25.5 ± 8.1 bpm) and the left CSS (-12.6 ± 4.3 bpm) was important (P<0.0001), as shown in Figure 2C.

In conclusion, our study shows that an acute fall in invasive systolic/ diastolic BP and HR are observed during the right and the left CSS. This effect is more intense to the right than the left CSS regarding the fall in the invasive systolic BP and the HR. These findings suggest the importance of the vagal tone as one of the mechanisms to suppress hypertension.

Conflict of interest
None declared.

Funding
This study was funded by Pacemed (US $200,000), Rio de Janeiro, Brazil.
Acknowledgements

The authors are grateful to all participants included in this study. The authors also thank Pacemed for stimulating the development of this study and for providing technical support.

References


Figure 2. Effects of the right (A) and the left (B) CSS in the heart rate, as well as, in the comparison between the variation (Δ) of heart rate (C) during the right and the left CSS. CSS, carotid sinus stimulation; N=18.