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Research Article

Effects of carotid body tumor resection on the blood pressure of essential hypertensive patients

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Abstract

Removal of carotid body (CB) improves animal models of hypertension (HTN) and heart failure, via withdrawal of chemoreflex-induced sympathetic activation. Effect of CB tumor (CBT) resection on blood pressure (BP) in subjects with HTN is unknown. A retrospective analysis of 20 subjects with HTN (BP≥140/90 mmHg or anti-hypertensives use) out of 134 with CBT resection. Short-term (30 days from surgery) and long-term (slope of regressions on time over the entire follow-up) changes in BP and heart rate were adjusted for covariates (interval between readings, total follow-up, number of readings and changes in therapy). Age and duration of HTN were 56±4 and 9±5 years. Adjusted short-term decreases in systolic (SBP: -9.9±3.1, $p<0.001$) and pulse pressures (PP: -7.9±2.7, $p<0.002$) were significant and correlated with their respective long-term changes (SBP: $r=0.47$, $p=0.047$; PP: $r=0.54$, $p=0.019$). There was a strong relationship between adjusted short-term changes in SBP and PP ($r=0.64$, $p<0.004$). Six (50% of responders or 33% of the total) had short-term falls of SBP ≥10 mmHg and of PP ≥ 5mmHg. First study to show that unilateral CBT resection is associated with sustained reduction of BP in hypertensive patients. Targeted CB chemoreflex removal could play a role in the therapy of human HTN. J Am Soc Hypertens 2015;9(6):435–442. © 2015 American Society of Hypertension. All rights reserved.

Keywords: Chemoreflex; hypertension; pulse pressure; sympathetic nervous system.

Introduction

The carotid bodies (CBs) are bilateral ovoid organs of 1.5–7.0 mm located at the carotid bifurcation and innervated by a parasympathetic (glossopharyngeal nerve) and sympathetic (superior cervical ganglion) nerve plexus. They are chemosensors for arterial oxygen, carbon dioxide, blood pH, blood glucose, and blood flow[1,2] via Type II glomus cells derived from the neural crest, and relay their information to the medulla oblongata, particularly for the control of respiration in response to hypoxia.

Activation of CB chemoreceptive cells is a powerful stimulator of the sympathetic nervous system, and their intermittent or chronic overactivity has been linked to development and progression of cardiovascular diseases such as hypertension (HTN) and heart failure (CHF).[3] In animal models, resection of the CB or inhibition of its output by hyperoxia improves HTN, CHF, and diabetes mellitus (DM).[4–7] In humans, the size of the CB correlates with the prevalence of sympathetically mediated diseases

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such as HTN, CHF, and DM,[8,9] CB hypersensitivity relates to increased mortality in CHF,[10] and hyperoxia improves hemodynamic characteristics of CHF[11]; hence, CB resection has been attempted as a possible treatment for patients with advanced CHF.[12]

In human essential hypertensive subjects: (1) the CBs are hypersensitive to chemical stimuli compared with those of their normotensive counterparts,[13] (2) surgical CB removal reduces blood pressure (BP) in subjects with comorbid asthma,[3,14] and (3) hyperoxia reduces BP in otherwise untreated subjects.[15,16] A pivotal single–arm, unblinded trial testing the effects of surgical and interventional CB resection on human resistant HTN is ongoing in Europe (clinicaltrials.gov identifier: NCT01745172/NCT02099851).

Tumors of the CB (CBTs) are rare (prevalence of 1–2 per 100,000), usually benign, and only rarely catecholamine–secreting (1%–5% of the cases[17,18]). Surgical resection of non–functional tumors removes the stimulatory effect of the chemoreflex on the sympathetic nervous system but is associated with opposing effects on sympathetic regulation by concomitant damage of the baroreflex. We took advantage of a large series of patients who underwent CBT resection by one of the authors (JLN) to assess the net effect of this intervention on BP in a subset of patients with pre–existing HTN.

Methods

We conducted a retrospective review of the medical records of 134 patients with uni– or bilateral resection of CBTs between 1990 and 2012 at the Vanderbilt Head and Neck Surgical Department. Institutional Review Board approval was obtained from the Vanderbilt University (IRB 131501). Only 20 subjects met the entry criterion of preceding HTN, defined as BP ≥140/90 mm Hg or use of anti–hypertensive drugs. Two of these subjects were excluded from analyses because of inadequate follow–up data. Two subjects had a subsequent surgical excision of a contralateral CBT. In these subjects, the study was limited to data after the first procedure, for uniformity among all subjects and to avoid including data in patients with baroreflex failure, a complication of bilateral CBT resection. Sixteen of the remaining 18 subjects were on anti–hypertensive medications, whereas the other two were not, despite meeting BP criteria for hypertension. Clinical and BP data were obtained by review of Vanderbilt's medical record, records of the patients' primary care providers, and telephone interviews. The average of all sphygmomanometric seated BPs obtained during the 3 months preceding surgery was used as the baseline BP. Short–term changes in systolic (ΔSBPst) and diastolic (ΔDBPst) BPs, pulse pressures (ΔPPst), and heart rates (ΔHRst) were calculated as the subtraction of this baseline from the first BP or HR reading obtained at least 30 days after the surgical procedure. BP readings obtained before 30 days from the surgical date were purposely discarded to minimize confounding effects of immediate postoperative BP variability. Long–term changes in BP and HR (ΔSBPlt, ΔDBPlt, ΔPPlt, and ΔHRlt) were estimated by the slope of the regression of these BPs and HRs on time, using all data available for the entire period of follow–up in each individual patient and are reported as the changes per year (mm Hg/y or beats per minute [bpm]/y).

Because of the retrospective nature of the study, there was large variability in time intervals between BP and HR readings, number of readings, duration of follow–up, and changes of medications during the short–term and long–term periods. Therefore, both the short–term BP changes and the long–term slopes were adjusted by use of covariate analyses. For short–term data, the covariates were: (1) the interval between baseline and postoperative readings, and (2) the change in therapy during this interval. For long–term data, the covariates were: (1) the total duration of follow–up, (2) the total number of readings during the study, and (3) the change in therapy from the beginning to the end of follow–up. Changes in therapy were quantified using a treatment intensity score for the baseline and each follow–up visit, based on a combination of maximum recommended daily dose for each medication according to the April 2014 Monthly Prescribing Reference[19] and equipotency of different antihypertensive agents (Supplemental Table S1).

Descriptive data are presented as means ± standard errors of the mean (SEM), percentages, or medians and quartiles as appropriate. Deltas of parameters before and after tumor resection were analyzed by paired Student *t*–tests. Correlations between parameters were assessed by Pearson correlation coefficients and simple linear regression analyses. Covariate analysis was carried out with multivariate regression for data in all subjects, entering the covariates as regressors in the form of a matrix (deviations from the mean for the employed continuous covariates). The beta coefficients for the covariates and the matrix covariates for each individual patient were used for calculation of adjusted y as previously reported.[20]

Results

Table 1 shows the baseline clinical characteristics of the 18 subjects analyzed in the study. Age was 56 ± 2 years, with an almost equal gender distribution (44% male and 56% female). Fourteen subjects were on antihypertensive therapy; baseline SBP and DBP were 141 ± 3/83 ± 3 mm Hg, and duration of known HTN was 9 ± 2 years. Body mass index (BMI) was 32.5 ± 3, with 12 of 18 subjects (66.7%) exceeding the cut–off for diagnosis of obesity (30 kg/m^2). Following resection, the average BMI increased