Comparison of nasal pH values in black and white individuals with normal and high blood pressure

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ABSTRACT

Salt-sensitive hypertension is common in people of African origin, and may be caused by increased transepithelial sodium absorption. The pH of nasal secretions is negatively correlated with the difference in Na\(^+\) concentration between nasal secretions and plasma, and may be a marker of transepithelial sodium absorption. Nasal pH was measured using a probe sited under the inferior turbinate. Measurements of nasal pH were reproducible, with a coefficient of variation of 3.3% for repeated measurements on the same day and of 2.7% between measurements on different days. Nasal pH did not correlate with nasal potential difference, a measure of transepithelial sodium absorption. Nasal pH was significantly lower in 89 black individuals (24 normotensive and 65 hypertensive) than in 51 white individuals (26 normotensive and 25 hypertensive) (black normotensive, 6.44 ± 0.08; black hypertensive, 6.62 ± 0.05; white normotensive, 6.91 ± 0.06; white hypertensive, 6.98 ± 0.06), after adjustment for age, gender, current smoking status, body mass index and 24 h urinary sodium excretion (P = 0.002), but was not significantly different between the normotensive and hypertensive individuals. Nasal pH was more acidic in black than in white individuals, which may represent generalized up-regulation of sodium transport in black people. However, the lack of correlation between nasal pH and potential difference suggests that nasal pH is, at best, only weakly related to transepithelial sodium absorption. Ethnic differences in nasal pH may be of direct relevance in the airways, as many of the functions of airway surface liquid are dependent on pH.

INTRODUCTION

Hypertension is common in people of African origin living in urban societies. Nearly half of middle-aged black U.K. residents and 76% of African Americans between the ages of 65 and 74 years have high blood pressure requiring treatment [1,2]. Blood pressure is generally more salt-sensitive in black people [3]. Black people with hypertension have suppressed plasma renin activity and angiotensin II levels [4], and excrete a sodium load more slowly and less completely than white people [5]. These features all suggest that a reduced ability of the kidney to excrete sodium may underlie the development of high blood pressure in black people.

Renal sodium transport cannot be measured directly, as the renal tubule is not accessible to clinical assessment. The airway epithelium shares many ion-transport proteins with the renal epithelium, is easily accessible in the nose and may be useful as a model of renal sodium transport. Measurements of trans-nasal potential difference have been used to demonstrate altered sodium channel activity in Liddle’s syndrome, a monogenic form
of hypertension caused by activating mutations of the epithelial sodium channel [6], and in pseudohypoaldosteronism type 1, a syndrome of low blood pressure caused by inactivating mutations of the epithelial sodium channel [7]. The pH of nasal secretions (nasal pH) may also provide a measure of transepithelial sodium absorption. Nasal pH is usually acidic relative to plasma pH [8,9]. In humans, nasal pH is negatively correlated with the difference in Na⁺ concentration between nasal secretions and plasma, suggesting that H⁺ excretion could be linked to Na⁺ absorption across the nasal epithelium [10]. This concept is supported by the finding that, in ferret tracheal secretions, again suggesting a link between H⁺ excretion and Na⁺ absorption across airway epithelia [11].

We hypothesize that increased transepithelial sodium transport contributes to the development of high blood pressure in black people. If nasal pH truly reflects transepithelial sodium transport, acidic nasal pH could be used as a marker for increased transepithelial sodium absorption. The aim of the present study was to investigate the relationship between nasal pH and sodium excretion. As assessed by measurements of nasal potential difference, and to compare nasal pH between black and white people with normal and high blood pressure.

**METHODS**

**Recruits**

**Validation of nasal pH measurement technique**

Individuals were recruited from staff at St George’s Hospital Medical School for repeat measurements of nasal pH. Ethnicity and blood pressure were not recorded in this group.

**Comparison of nasal pH in black and white individuals with normal and high blood pressure**

Hypertensive individuals were taken from unselected referrals by local general practitioners to the hypertension clinic. Normotensive controls were volunteers from the local population recruited by advertisement, or non-consanguineous relatives of hypertensive patients attending the Blood Pressure Unit at St George’s Hospital. All individuals had their blood pressure measured using an Omron HEM-705CP oscillometric blood pressure recorder [12]. Individuals rested for 5 min, after which blood pressure recordings were done in triplicate using the appropriate cuff size based on the upper mid-arm circumference. Blood pressure values given are the means of these three recordings. Hypertensive individuals had a systolic blood pressure of > 140 mmHg and/or a diastolic blood pressure of > 90 mmHg. Normotensive individuals had a systolic blood pressure of ≤ 140 mmHg and a diastolic blood pressure of ≤ 90 mmHg. Hypertensive individuals had not received previous treatment, or had been off all drug treatment for at least 2 weeks and diuretics for 4 weeks. People with ischaemic heart disease, cerebrovascular disease, renal impairment or other concurrent illness were excluded from the study. Ethnicity was defined by skin colour, place of birth or parents’ birth and cultural identity. Where individuals were classified as ‘black’, African or Caribbean ancestry was also noted.

In all studies of nasal pH measurement, individuals were excluded from the study if they had any evidence of acute or chronic rhinitis, asthma or atopy, or took nasal drugs or any other drug that might interfere with nasal epithelial function. Written informed consent was obtained from all individuals prior to entry into the study, which was approved by the Local Research Ethics Committee of Merton, Sutton and Wandsworth. Procedures followed were in accordance with institutional guidelines.

**Clinical measurements**

All individuals collected a 24 h urine sample 1–2 days before attendance for nasal pH measurement, and this was analysed for 24 h excretion of urinary sodium, potassium and creatinine. On the day of nasal pH measurement, individuals attended the Blood Pressure Unit having had water, but no food or other beverages from midnight onwards. Blood pressure, weight and height were recorded. Smoking history was taken to determine whether the subject had never smoked, was an ex-smoker or was a current smoker. Serum sodium, potassium, creatinine and urea were measured. Plasma was analysed for plasma renin activity and plasma aldosterone concentrations by RIA [13,14]. Individuals then underwent measurement of nasal pH and nasal potential difference.

**Measurement of nasal pH**

Measurements of nasal pH were obtained using a portable pH meter (Type 93-8052; Synectic Medical) and a nasal pH probe (Type LoT440; Synectic Medical). The nasal pH probe consisted of a single glass probe of 3 mm diameter, containing both reference and sensing electrodes. Before measuring pH in each subject, the probe was calibrated using buffered solutions of pH 7.01 and pH 1.01. The probe was sited under the inferior turbinate of the right nostril. If the right nostril could not be cannulated because of septal deviation, the left nostril was used. pH was recorded at a depth of 4 cm from the anterior nares until readings were stable for ≥ 10 s. All
readings were made by one of two operators. Operators were not blinded to the ethnicity or blood pressure status of individuals.

Validation of nasal pH measurement technique
To determine the repeatability and reliability of pH measurements, individuals recruited for this part of the study had nasal pH measured on two separate visits. On the first visit, measurement of pH was carried out three times in the same nostril, with the probe being washed in distilled water between each recording. At a second visit, at the same time on the next day, three measurements of nasal pH were obtained in the same nostril using the same protocol.

Comparison of nasal pH in black and white individuals with normal and high blood pressure.
Black and white normotensive and hypertensive individuals each underwent one measurement of nasal pH between 09.00 and 14.00 hours.

Measurement of nasal potential difference
Measurements of nasal potential difference were carried out in black and white normotensive and hypertensive individuals in the same nostril after measurement of nasal pH was completed. Measurements were made by one of two operators using the same set of equipment. Operators were not blinded to the blood pressure status of the individuals. Transmucosal nasal potential difference was measured by a technique established previously in our laboratory [15]. The reference electrode consisted of a 23 G butterfly needle, which was inserted into the subcutaneous tissue of the forearm. The exploring electrode was an 8 G nasogastric tube filled with Ringer’s solution, which was introduced along the inferior surface of the inferior turbinate to a distance of 7 cm. Both electrodes were connected to a high-impedance voltmeter by 1% Ringer’s agar bridges. The output of the voltmeter was recorded continuously on a chart recorder throughout the experiment. Nasal potential difference was recorded from the inferior surface of the inferior turbinate as the exploring electrode was withdrawn. The site of maximum potential difference was established, and the measurement at this site was recorded once the voltage had been stable for more than 5 s. A second measurement of the maximum potential was made at the same site to ensure consistency of recording, and the mean of these two maximum values was taken as the potential difference for analysis. Values were lumen-negative with respect to the submucosa.

Statistical analysis
Group values are given as mean±S.E.M. for normally distributed data, and as median and interquartile range for plasma renin activity and aldosterone concentration, which are not normally distributed. Two-way ANOVA was used to compare nasal pH between black and white individuals, and between normotensive and hypertensive individuals, before and after adjustment for age, gender, body mass index (BMI), smoking status and 24 h urinary sodium excretion. The difference in nasal pH between ethnic groups was examined further using Student’s paired t test to compare nasal pH between subgroups of 15 black individuals and 15 white individuals (10 hypertensive and five normotensive in each group) matched for age, gender, BMI and blood pressure. Other differences between groups were tested using two-sample t-tests for normally distributed variables and chi-squared tests for categorical variables. Pearson correlation coefficients were calculated to examine relationships between nasal pH and nasal potential difference, blood pressure and biochemical variables within black and white normotensive and hypertensive groups. Two-tailed P values of < 0.05 were considered significant.

RESULTS
Validation of the nasal pH measurement technique
To assess the repeatability and reliability of nasal pH measurements, 20 individuals underwent three repeat pH measurements on each of two consecutive days. The average coefficient of variation for repeated measurements on the same day was 3.3%, and that between days was 2.7%. These results suggest that pH measurements are reasonably stable when recorded in an individual in the same setting, and are consistent for the same person on different days.

Comparison of nasal pH in black and white normotensive and hypertensive individuals.
Groups of 24 black normotensive individuals, 65 black hypertensive individuals, 26 white normotensive individuals and 25 white hypertensive individuals were studied. The demographic characteristics of individuals are shown in Table 1, and biochemical measurements are shown in Table 2.

Nasal pH measurements
Nasal pH was more acidic in black than in white individuals (black normotensive, 6.44±0.08; black hypertensive, 6.62±0.05; white normotensive, 6.91±0.06; white hypertensive, 6.98±0.06) (Table 3). Two-way ANOVA showed that nasal pH was significantly more acidic in black than in white individuals (P < 0.0001), but was not significantly different between normotensive and hypertensive individuals. The difference in pH between
black and white individuals remained significant after adjustment for age, BMI, gender and smoking status ($P = 0.002$). The distribution of nasal pH values in black and white individuals is shown in Figure 1. Further analysis showed that nasal pH was not significantly different between black people of African ancestry and black people of Caribbean ancestry [African, $6.63 \pm 0.06$ ($n = 28$); Caribbean, $6.56 \pm 0.06$ ($n = 48$); $P = 0.43$].

To confirm the relationship between nasal pH and ethnic group, nasal pH measurements were compared between subgroups of 15 black individuals and 15 white individuals (10 hypertensive and five normotensive sub-

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**Table 1. Clinical characteristics of black and white individuals with normal and high blood pressure**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Black ethnicity</th>
<th>White ethnicity</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Normotensive</td>
<td>Hypertensive</td>
</tr>
<tr>
<td>Number</td>
<td>24</td>
<td>65</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female (%)</td>
<td>(62.5)</td>
<td>(66.2)</td>
</tr>
<tr>
<td>Age (years)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Males</td>
<td>$41.7 \pm 4.8$</td>
<td>$46.6 \pm 2.5$</td>
</tr>
<tr>
<td>Females</td>
<td>$43.7 \pm 2.9$</td>
<td>$49.5 \pm 1.7$</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>$28.26 \pm 0.87$</td>
<td>$29.37 \pm 0.58$</td>
</tr>
<tr>
<td>Systolic BP (mmHg)</td>
<td>$77.7 \pm 1.5$</td>
<td>$101.8 \pm 1.3$</td>
</tr>
</tbody>
</table>

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**Table 2. Biochemical characteristics of black and white individuals with normal and high blood pressure**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Black ethnicity</th>
<th>White ethnicity</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Normotensive</td>
<td>Hypertensive</td>
</tr>
<tr>
<td>Sodium (mmol/l)</td>
<td>$138.8 \pm 0.29$</td>
<td>$139.4 \pm 0.23$</td>
</tr>
<tr>
<td>Potassium (mmol/l)</td>
<td>$4.26 \pm 0.07$</td>
<td>$4.11 \pm 0.09$</td>
</tr>
<tr>
<td>Creatinine (mmol/24 h)</td>
<td>$13.4 \pm 0.8$</td>
<td>$13.7 \pm 0.6$</td>
</tr>
<tr>
<td>Urea (mmol/24 h)</td>
<td>$132.0 \pm 1.4$</td>
<td>$135.0 \pm 2.5$</td>
</tr>
<tr>
<td>Plasma renin activity (ng/ml⁻¹·h⁻¹)</td>
<td>$0.31 \pm 0.01$</td>
<td>$0.16 \pm 0.01$</td>
</tr>
<tr>
<td>Aldosterone (pmol/l)</td>
<td>$317 \pm 100$</td>
<td>$342 \pm 255$</td>
</tr>
</tbody>
</table>

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**Table 3. pH and calculated H⁺ concentration of nasal secretions in black and white normotensive and hypertensive individuals**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Black</th>
<th>White</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Normotensive</td>
<td>Hypertensive</td>
</tr>
<tr>
<td>pH of nasal secretions</td>
<td>$6.44 \pm 0.08$</td>
<td>$6.62 \pm 0.05$</td>
</tr>
</tbody>
</table>
| H⁺ concentration (nmol/l) | $363 \pm 102$ | $240 \pm 214$ | $123 \pm 107$ | $105 \pm 91$
Ethnic differences in nasal pH values

Figure 1  Distribution of nasal pH values in black and white individuals

Table 4  Clinical characteristics of 15 white individuals and 15 black individuals matched for age, gender, BMI and blood pressure
Values are means ± S.E.M. BP, blood pressure.

<table>
<thead>
<tr>
<th>Variable</th>
<th>African/Caribbean (n = 15)</th>
<th>Caucasian (n = 15)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male:female</td>
<td>10:5</td>
<td>10:5</td>
</tr>
<tr>
<td>Age (years)</td>
<td>51.6 ± 2.3</td>
<td>51.9 ± 2.4</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>27.4 ± 0.8</td>
<td>27.6 ± 1.2</td>
</tr>
<tr>
<td>Systolic BP (mmHg)</td>
<td>154.3 ± 5.9</td>
<td>150.1 ± 7.0</td>
</tr>
<tr>
<td>Diastolic BP (mmHg)</td>
<td>94.3 ± 3.7</td>
<td>90.9 ± 4.2</td>
</tr>
</tbody>
</table>

jects in each group) matched for age, gender, BMI and blood pressure. Clinical characteristics of these matched groups are shown in Table 4. Nasal pH was significantly more acidic in the 15 black individuals than in the 15 white individuals (black, 6.59 ± 0.11; white, 6.94 ± 0.07; P = 0.011).

Nasal pH and smoking status
Smoking status differed between the ethnic groups. Significantly more white than black individuals were current or ex-smokers (white, 68.4%; black, 22.5%; P < 0.0001) (Table 1).

Observed differences in nasal pH between black and white individuals were not accounted for by differences in smoking status. Nasal pH was more acidic in black than in white individuals when grouped by smoking history (Figure 2). Nasal pH was significantly more acidic in black than in white individuals after adjustment for current smoking status, as well as for age, gender, BMI and 24 h urinary sodium excretion (P = 0.002).

Relationship between nasal pH and other variables
Within each of the four groups of black and white normotensive and hypertensive individuals, there was no correlation between nasal pH and nasal potential difference, or between nasal pH and blood pressure, serum biochemistry, 24 h urinary sodium or potassium excretion, or plasma hormone activity or concentration.

DISCUSSION
Our results show that nasal secretions are more acidic in black people as a group than in white people. If nasal pH truly is a surrogate measure of transepithelial sodium absorption, then our findings suggest that sodium absorption is greater in black than in white people. In the design of this study, we made two assumptions: that nasal pH measurements could be used as a surrogate marker for sodium absorption, and that nasal sodium transport reflects renal sodium transport. In the interpretation of our results, it is first important to consider the validity of these assumptions.

Nasal pH is usually acidic relative to plasma pH [8,9]. The maintenance of the pH of nasal secretions depends on intact nasal epithelium; nasal pH rises to more alkaline values where the epithelium is damaged by infective or allergic rhinitis [16]. The mechanisms by which nasal secretions are made acidic, however, are not clear. Nasal pH has been linked to sodium transport. In humans the sodium gradient from nasal secretions to plasma is negatively correlated with the pH of the nasal secretions. This suggests that the greater the trans-nasal absorption of sodium, the more acidic is the nasal pH [10]. In ferret trachea, stimulation of the secretion of airway surface liquid using methacholine causes both an increase in H⁺ concentration and a decrease in Na⁺ concentration of tracheal secretions, again suggesting a link between increased Na⁺ absorption across airway epithelium and more acidic airway secretions. [11]. The predominant

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mechanism of sodium absorption across the airway epithelium is through apical sodium channels. This process generates a lumen-negative potential difference that could drive the passive secretion of H\(^+\) ions, hence linking increased sodium absorption with a fall in the pH of airway secretions [17]. However, in the present study we found no correlation between nasal pH and nasal potential difference values in either ethnic group. These observations suggest that sodium absorption through epithelial sodium channels does not determine the pH of nasal secretions. Other sodium transport processes described in airway epithelium, such as Na\(^+\)/H\(^+\) exchangers [18] and Na\(^+\)/HCO\(_3\)\(^-\) co-transporters [19], could also link increased Na\(^+\) absorption with increasing acidity of airway secretions. However, the contribution of these transporters to overall sodium absorption is likely to be small, and is unlikely to result in a good correlation between sodium absorption and nasal pH. The assumption that nasal pH measurements reflect sodium absorption has not been explored further in the present study, and requires future elucidation.

Nasal measurements of sodium transport can provide some information about renal sodium transport. Where sodium transporters are expressed in both the renal tubule and the nasal epithelium, measurement of transporter activity in the nose could directly reflect activity of that transporter in the kidney. For example, the epithelial sodium channel is expressed in both the renal and nasal epithelia [20,21]. Activating mutations of this channel in Liddle’s syndrome result in increased renal tubular sodium absorption and hypertension, which can also be detected in the nose as increased nasal potential difference [6]. Inactivating mutations of the epithelial sodium channel in pseudohypoaldosteronism type 1 result in decreased renal tubular sodium absorption with low blood pressure, and can be detected in the nose as decreased nasal potential difference [7]. Other sodium transporters expressed both in renal [22] and airway [17] epithelia include Na\(^+\)/H\(^+\) exchangers, Na–K–ATPase pumps and Na–K–2Cl co-transporters. It is probable that structural abnormalities in these transporters would also result in a change of transporter function in both nasal and renal epithelia. The use of nasal measurements as a surrogate for renal sodium transport does have limitations. Although similar sodium transport proteins are found in both the nose and the kidney, the transporters are regulated differently and hence may function differently in the two tissues.

We have used nasal pH measurements to explore the hypothesis that increased sodium absorption contributes to the development of high blood pressure in black people. Nasal pH did not correlate with nasal potential difference, and therefore at best can be linked only weakly to transepithelial sodium absorption. In the light of this, few conclusions can be reached about the pathogenesis of hypertension from the present study.

Nasal pH was more acidic in black than in white subjects, perhaps reflecting up-regulation of sodium absorption in black people as a group. Although there was no difference in nasal pH between hypertensive and normotensive people within ethnic groups, and no correlation between nasal pH and blood pressure, it is possible that most black people have up-regulation of sodium transport, as evinced by low nasal pH, but that the timing of the development of hypertension depends on individual exposure to precipitants such as high salt intake, low potassium intake or other factors, such as obesity.

Our finding that black people as a group have more acidic nasal secretions than white people may, however, be of direct relevance in the airways. The pH of nasal secretions is similar to the pH of surface liquid in the lower airways [11,23], and many of the functions of airway surface liquid are dependent on pH. For example, acidic pH may confer an advantage in lung defence by promoting the activity of lysozyme in airway surface liquid [24] and inhibiting bacterial adhesion to airway epithelial cells [25]. Conversely, the ability of antioxidants to scavenge free radicals (e.g. from ozone) is impaired by an acidic pH [26]. The relevance of the pH of airway secretions to the development of pulmonary disease requires further elucidation.

ACKNOWLEDGMENTS

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