Reference values for sniff nasal inspiratory pressure in healthy subjects in Brazil: a multicenter study*,**

Valores de referência da pressão inspiratória nasal em indivíduos saudáveis no Brasil: estudo multicêntrico

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Abstract

Objective: The objectives of this study were to determine reference values for sniff nasal inspiratory pressure (SNIP) and to propose reference equations for the population of Brazil. **Methods:** We evaluated 243 healthy individuals (111 males and 132 females), between 20 and 80 years of age, with an FVC and FEV_1/FVC ratio > 80% and > 85% of the predicted value, respectively. All of the subjects underwent respiratory muscle strength tests to determine MIP, MEP, and SNIP. **Results:** We found that SNIP values were higher in males than in females ($p < 0.05$) and that SNIP correlated negatively with age, for males ($r = -0.29$; $p < 0.001$) and for females ($r = -0.33$; $p < 0.0001$). Linear regression also revealed that age influenced the predicted SNIP, for males ($R^2 = 0.09$) and females ($R^2 = 0.10$). We obtained predicted SNIP values that were higher than those obtained for other populations. **Conclusions:** We have devised predictive equations for SNIP to be used in adults (20-80 years of age) in Brazil. These equations could help minimize diagnostic discrepancies among individuals.

Keywords: Respiratory Muscles; Respiratory Function Tests; Reference Values; Linear Models.

Resumo

Objetivo: Os objetivos do presente estudo foram determinar equações de referência para pressão inspiratória nasal (PIN) e propor equações de referência para a população brasileira. **Métodos:** Foram avaliados 243 indivíduos saudáveis (111 homens e 132 mulheres), entre 20 e 80 anos, com CVF > 80% e razão VEF_1/CVF > 85% do predito. Todos os indivíduos realizaram testes de força muscular respiratória para a determinação de PIN, PImáx e PEmáx. **Resultados:** Os valores da PIN foram maiores no sexo masculino que no feminino ($p < 0,05$), e a PIN apresentou correlação negativa com a idade para homens ($r = -0,29$; $p < 0,001$) e mulheres ($r = -0,33$; $p < 0,0001$). A análise de regressão linear múltipla também revelou que a idade permaneceu exercendo influência na predição da PIN em homens ($R^2 = 0,09$) e mulheres ($R^2 = 0,10$). Os valores preditos da PIN encontrados foram superiores àqueles obtidos em outras populações. **Conclusões:** Nesse contexto, sugerem-se equações preditivas para PIN em indivíduos brasileiros saudáveis na faixa etária entre 20 e 80 anos, com o intuito de minimizar discrepâncias diagnósticas ao comparar indivíduos.

Descritores: Músculos Respiratórios; Testes de Função Respiratória; Valores de Referência; Modelos Lineares.

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Introduction

In individuals with lung, heart, or neuromuscular disease, respiratory muscle dysfunction is often associated with pulmonary complications, elevated morbidity indices, impaired quality of life, and mortality.[1] Respiratory muscle assessment is a relevant method for the early detection of such dysfunction and the quantification of its decline, providing prognostic and predictive information on the survival of these patients.[1-3]

The determination of sniff nasal inspiratory pressure (SNIP) is an easily applied, noninvasive volitional technique that has been recommended as a test to complement the evaluation of inspiratory muscle strength (by determining MIP). Combining inspiratory muscle tests can significantly improve the accuracy of a diagnosis of inspiratory muscle weakness.[4-6]

Normal respiratory muscle strength values are useful for establishing, interpreting, and diagnosing respiratory muscle dysfunction.[6,7] Given the specific biological characteristics of regional populations, reference values must be obtained from healthy male and female subjects within a given region, in order to avoid diagnostic discrepancies when individuals or populations are compared.[8] Although predicted values of SNIP have been established for healthy White adults,[6] Japanese adults,[9] and White children,[10] such values have yet to be established for healthy adults in Brazil.

The primary objectives of this study were to determine SNIP reference values for a population of healthy adults in Brazil; to compare maximum SNIP values between males and females and between age brackets; and to propose reference equations for the determination of SNIP in Brazil.

Methods

A multicenter, observational, cross-sectional study was carried out between 2009 and 2011 at three research centers. Subjects were stratified into six age brackets (20-29 years, 30-39 years, 40-49 years, 50-59 years, 60-69 years, and 70-80 years). As in earlier studies,[6,11] subjects in each age bracket were also divided by gender, in order to determine gender-specific reference values. Individuals were assessed in terms of sociodemographic data, life habits, previous or current diseases, anthropometric parameters (weight, height, and body mass index [BMI]), and lung function (as assessed by spirometry). Study participants were also assessed for respiratory pressures (MIP and MEP), SNIP and habitual pattern of physical activity. At each research center, a single examiner performed the assessment on a single day. Weight and height were measured with an anthropometric scale (Filizola®, São Paulo, Brazil). We determined BMI using the following formula: BMI = weight in kilograms/height in meters squared (kg/m²).[12]

The sample was composed of individuals from the cities of Natal (in the state of Rio Grande do Norte), Recife (in the state of Pernambuco) and Piracicaba (in the state of São Paulo). The inclusion criteria were being healthy, being a non-athlete, being between 20 and 80 years of age,[6] having a BMI between 18.5 and 29.9 kg/m², and being a non-smoker.[8] Subjects with a history of respiratory disease (asthma, chronic bronchitis, tuberculosis, COPD, or emphysema) were excluded, as were those with a history of neuromuscular disease, cerebrovascular, or cardiac disease (myocardial infarction or heart failure)[8,13,14]; those with rhinitis, sinusitis, or deviated septum; those having previously undergone nasal surgery; those having had a cold or the flu in the last week[11]; those regularly using medication to treat respiratory allergies; those taking oral corticosteroids, central nervous system depressants, barbiturates, or muscle relaxants[14,15]; those who were pregnant[9]; those with an FVC ≤ 80% of the predicted value; and those with an FEV_1/FVC ratio ≤ 85% of the predicted value.[6] Individuals incapable of understanding or performing the maneuvers required for assessment were also excluded from the study. None of the participants had previously been exposed to respiratory muscle strength measuring techniques. The study was approved by the Research Ethics Committee of the Onofre Lopes University Hospital (Protocol no. 260/08), and all subjects gave written informed consent. All procedures were conducted in accordance with the ethical standards set forth in the Declaration of Helsinki.[16]

Spirometry was conducted with a DATOSPIR-120C® spirometer (Sibelmed, Barcelona, Spain), properly calibrated, and all spirometric tests were conducted in accordance with American Thoracic Society/European Respiratory Society (ATS/ERS) guidelines.[17] We determined FVC, FEV_1 and the FEV_1/FVC ratio. Results (obtained in absolute and relative values) were compared with previously published reference values.[18]

Respiratory muscle strength was assessed on the basis of maximal respiratory pressures (MIP and MEP). After having been instructed in the procedure, subjects were evaluated using a MicroRPM® digital manometer (Micro Medical, Rochester, UK), and tests were conducted in accordance with ATS/ERS[4] norms and recommendations. Results were obtained in absolute values and compared with previously published reference values.[11] We measured MIP with a disposable cylindrical mouthpiece connected to the manometer. Subjects were asked to perform a maximal inspiratory maneuver from RV. To assess MEP, we instructed subjects to perform a maximal expiratory maneuver from TLC.

To evaluate SNIP, the subject remained seated, with one nostril occluded by a silicon nasal plug connected to the MicroRPM® digital manometer by a polyethylene catheter (internal diameter, ≈ 1 mm). We measured SNIP from functional residual capacity (FRC). With their mouths closed, subjects performed a maximal sniff maneuver through the contralateral patent nostril at the end of a slow, normal expiration.[4,6,11] Ten maneuvers were executed.[6,19] The criteria used to select the best technically acceptable sniffs include a maneuver with a peak pressure maintained for less than 0.5 s and a 30-s rest period between maneuvers. We used the Puma computer program (The University of Manchester, Manchester, UK), which automatically identifies acceptable maneuvers, and saved the values in a database. No visual feedback was provided during the maneuvers, and the highest value obtained was used in the data analysis.

We administered the Brazilian Portuguese-language version of Baecke's questionnaire for the measurement of habitual physical activity (HPA), which has been cross-culturally adapted and validated for use in Brazil.[20] The questionnaire evaluates individual perceptions regarding leisure-time physical activities, as well as leisure and locomotion in the last 12 months. Responses are scored on a 0-5 point scale, and scores are expressed as a summed index.

Sample size was calculated using a t-test based on mean population and maximum standard deviation of SNIP found in a study conducted by Uldry & Fitting,[6] and values of $p < 0.05$ (at a power of 99% with a confidence interval of 5%) were considered statistically significant. The suggested sample size was 260 individuals, with an expected interclass correlation coefficient of 7.86 cmH_2O. Data were expressed as mean ± standard deviation. We applied the Kolmogorov-Smirnov test for normality in order to determine data distribution. We compared MIP, MEP and SNIP values between genders using unpaired t-tests and between age brackets with ANOVA. If a significant F ratio was obtained, post-test comparisons were conducted with the Newman-Keuls test. Pearson's correlation coefficient was applied in order to correlate SNIP with the study variables. Linear regression analysis was used in order to obtain predictive equations for independent variables that correlated with SNIP. The lower limits of the regression model were calculated from the 5th percentile of the residual standard deviation, assuming a Gaussian distribution, and were estimated as follows[21]:

$$\textit{lower limit} = \textit{predicted value} - 1.645 \times \textit{SEE}$$

where *SEE* is the standard error of the estimate.

The probability of a type I error was set at 0.05 for all tests. Statistical analyses were performed with the Statistical Package for the Social Sciences, version 15 (SPSS Inc., Chicago, IL, USA).

Results

The volunteers were recruited from the community and assessed in a preliminary interview, as can be seen in Figure 1. Demographic characteristics, lifestyle, anthropometric parameters, and spirometric data are detailed in Table 1.

The respiratory pressure values are presented in Table 2. Overall, the mean values of MIP, MEP, and SNIP were significantly higher in males than in females (114.3 ± 28.6 cmH_2O vs. 92.6 ± 19.7 cmH_2O; $p < 0.05$). We also found that, within each gender, there were significant differences between age brackets ($p < 0.05$), as demonstrated in Table 2. Correlations between SNIP and the study variables are presented in Table 3. We found that SNIP correlated negatively with age, for males ($r = -0.29$; $p < 0.001$) and females ($r = -0.33$; $p < 0.0001$). However, SNIP did not correlate significantly with weight, height, BMI or HPA, for either gender. After linear regression, the only variable that maintained its significance was age, which was found to be predictive of SNIP, for males ($p < 0.001$) and for females ($p < 0.0001$), and was therefore included in

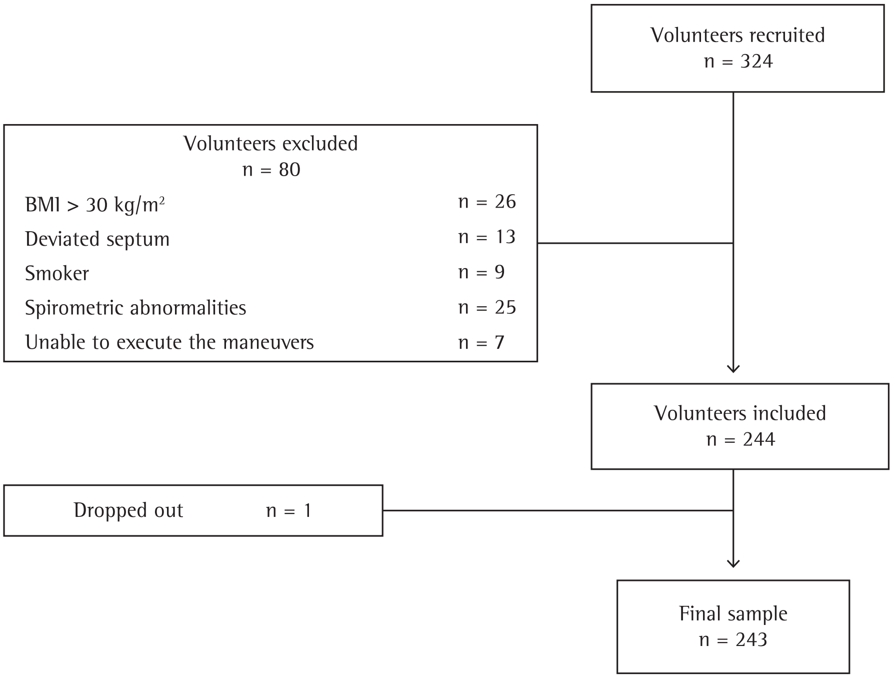

Figure 1 – Flow diagram of the selection of volunteers. BMI: body mass index.

Table 1 – Anthropometric and spirometric data, by age bracket within genders.[a]

Gender/Age bracket, years	Age	Weight, kg	Height, m	BMI, kg/m^2	HPA	FVC, % pred	FEV$_1$, % pred	FEV$_1$/FVC%
Males								
20-29	22.1 ± 2.2	73.9 ± 10.6	1.75 ± 0.09	24.1 ± 2.4	5.2 ± 1.3	89.7 ± 10.4	92.1 ± 10.9	103.0 ± 9.1
30-39	34.4 ± 3.4	76.3 ± 8.5	1.75 ± 0.04	25.0 ± 2.6	4.8 ± 1.3	94.1 ± 9.2	95.0 ± 10.2	101.5 ± 8.6
40-49	44.2 ± 2.6	75.6 ± 9.0	1.70 ± 0.06	26.0 ± 2.6	5.0 ± 1.7	94.3 ± 9.7	95.8 ± 11.3	101.6 ± 8.2
50-59	53.4 ± 2.8	77.1 ± 10.8	1.72 ± 0.06	26.0 ± 2.9	5.2 ± 1.2	92.7 ± 10.2	96.6 ± 12.2	104.5 ± 8.1
60-69	63.9 ± 2.6	74.6 ± 9.0	1.65 ± 0.09	27.4 ± 1.7	5.1 ± 1.6	91.8 ± 10.7	98.6 ± 12.3	107.6 ± 6.0
70-80	74.6 ± 4.0	71.4 ± 7.2	1.66 ± 0.08	26.0 ± 2.1	4.7 ± 1.0	90.2 ± 9.7	97.1 ± 10.9	108.1 ± 6.8
Females								
20-29	23.2 ± 3.3	61.9 ± 10.8	1.65 ± 0.06	22.8 ± 3.3	4.7 ± 0.1	92.3 ± 11.1	95.7 ± 13.6	97.8 ± 12.2
30-39	33.5 ± 3.2	62.6 ± 7.4	1.63 ± 0.05	23.6 ± 2.2	4.4 ± 1.2	97.7 ± 14.9	98.7 ± 14.1	99.4 ± 11.5
40-49	45.1 ± 3.4	63.6 ± 9.7	1.60 ± 0.07	24.9 ± 3.5	4.5 ± 1.5	98.4 ± 9.5	101.9 ± 10.0	100.0 ± 9.7
50-59	54.5 ± 3.5	63.3 ± 7.3	1.58 ± 0.06	25.5 ± 2.9	4.5 ± 1.3	90.4 ± 11.0	93.2 ± 11.7	99.5 ± 12.1
60-69	64.3 ± 3.1	65.2 ± 8.1	1.57 ± 0.07	26.5 ± 2.8	4.6 ± 1.2	96.7 ± 18.2	98.4 ± 10.3	102.2 ± 17.2
70-80	74.8 ± 3.2	65.2 ± 9.3	1.58 ± 0.07	25.9 ± 2.7	4.6 ± 0.8	95.5 ± 15.8	107.9 ± 20.5	108.4 ± 13.0

BMI: body mass index; HPA: habitual physical activity; and pred: of the predicted value. [a]Data are presented as mean ± SD.

the model to devise the predictive equations for SNIP as a function of age (Table 4):

Males: $SNIP = 135.6 - 0.47 \times (age)$ ($R^2 = 0.09$; $SEE = 27.4$)

Females: $SNIP = 110.1 - 0.36 \times (age)$ ($R^2 = 0.10$; $SEE = 18.6$)

where R^2 is the coefficient of determination. The mean lower limits are calculated by subtracting

Table 2 - Respiratory pressures, by age bracket within genders.[a]

Gender/Age bracket, years	n	Respiratory pressures		
		MIP, cmH_2O	MEP, cmH_2O	SNIP, cmH_2O
Males	111	111.0 ± 28.0[+]	149.6 ± 40.3[+]	114.3 ± 28.6[+]
20-29	27	119.2 ± 33.7[+]	152.6 ± 47.8[+]	118.6 ± 35.2
30-39	19	125.3 ± 23.8[+]	166.2 ± 39.2[+]	133.5 ± 25.9[+]
40-49	19	115.6 ± 26.3[+]	164.1 ± 42.7[+]	109.4 ± 25.3
50-59	16	107.6 ± 16.2[+]	150.2 ± 26.4[+]	122.4 ± 17.8[*,+]
60-69	16	91.6 ± 17.6[*]	131.8 ± 30.1	95.3 ± 20.7[*]
70-80	14	93.8 ± 25.5[*]	117.1 ± 18.6	99.3 ± 20.3[*]
Females	132	87.9 ± 17.6	106.7 ± 25.2	92.6 ± 19.7
20-29	25	96.9 ± 14.0	117.0 ± 27.7	102.8 ± 26.8
30-39	20	94.5 ± 18.3	111.2 ± 19.8	94.6 ± 19.9
40-49	24	90.2 ± 16.7	115.1 ± 26.1	97.6 ± 18.7
50-59	24	82.7 ± 17.0[*]	95.4 ± 23.7	88.0 ± 19.2
60-69	19	83.2 ± 19.7[*]	103.3 ± 26.5	86.6 ± 9.2
70-80	20	78.1 ± 13.4[*]	95.8 ± 17.1	82.9 ± 9.3

SNIP: sniff nasal inspiratory pressure. [a]Data are presented as means ± SD. *Significant effect between age brackets within the same gender ($p < 0.05$). +Significant effect between genders within the same age bracket ($p < 0.05$).

Table 3 - Correlations between SNIP and independent variables, by gender.[a]

SNIP	Age, years	Weight, kg	Height, m	BMI, kg/m^2	HPA
Males	−0.29[*]	0.12	0.13	0.02	0.12
Females	−0.33[+]	0.02	0.08	−0.02	0.11

SNIP: sniff nasal inspiratory pressure; BMI: body mass index; and HPA: habitual physical activity. [a]Values are r. *$p < 0.001$; +$p < 0.0001$.

Table 4 - Linear regression analysis of SNIP in males and females between 20 and 80 years of age.

Parameter	Gender	
	Male	Female
Mean SNIP, cmH_2O	114.3	92.6
R^2	0.09	0.10
SEE	27.4	18.6
p value	0.001	0.0001
Predictive equation	SNIP = 135.6 − 0.47 × (age)	SNIP = 110.1 − 0.36 × (age)
Mean lower limit[a]	69.2	61.9

SNIP: sniff nasal inspiratory pressure; SEE: Standard error of the estimate. [a]The mean lower limits were calculated by subtracting 1.645 times the residual SD of the mean.

1.645 times the residual standard deviation of the mean.

Discussion

The objectives of the present study were to determine reference values for SNIP in a population of healthy adults in Brazil; to compare maximum SNIP values between males and females, as well as between age brackets; and to propose reference equations for SNIP in Brazilians. Our results show that age has a negative influence on SNIP, as well as being a predictor of SNIP, and should therefore be included in linear regression equations to determine reference values.

Several studies have mentioned the importance of SNIP as a valid, non-invasive, easy-to-apply test of inspiratory muscle strength, as well as a complement to MIP.[5,6] This is the third study in the literature to propose reference values for SNIP in healthy adults and the first to do so for the Brazilian population. The results of the present study show that SNIP was significantly lower in females than in males, a finding that is likely due to the greater muscle mass of the latter, corroborating the findings of other studies investigating respiratory muscle strength.[11,21,22] In terms of SNIP values, we found significant differences between age brackets (within each gender) and a decrease with age. This might be attributed to the reduction in inspiratory muscle strength during the aging process, resulting from sarcopenia; the loss of muscle mass[22-24]; and the loss of viscoelasticity of the lungs and rib cage,[23] associated with an increase in abdominal fat, which can interfere with the biomechanics of the diaphragm.[11] Among the independent variables (age, weight, height, BMI, and HPA), only age correlated with SNIP (a weak negative correlation), which is in agreement with the findings of Uldry & Fitting[6] and, for males only, of Kamide et al.[9] Uldry & Fitting[6] also found that weight and BMI did not correlate with SNIP. Although respiratory muscle strength is directly related to the level of physical activity,[11] HPA showed no correlation with SNIP in either males or females. It should be borne in mind that Baecke's questionnaire provides only an index, which precludes characterizing the level of physical activity, thereby making it difficult to identify sedentary lifestyles.[25] The SNIP reference values obtained in the present study differed from those reported for healthy Japanese males and females (76.8 ± 28.9 cmH_2O and 60 ± 20 cmH_2O, respectively). Our linear regression analysis demonstrated that predictive equations resulted from SNIP as a function of age, for both genders, which is in keeping with the findings of Uldry & Fitting[6] and Kamide et al.,[9] except that the latter group of authors found that, in females, SNIP correlated only with BMI. This is in contrast with the reported negative influence of age on respiratory muscle strength,[21-23] as well as with the positive relationship between respiratory muscle mass and lean mass, which is more evident in males.[11,21] One important aspect of our results is that the coefficient of determination for age in the linear regression model was low, for males and females (R^2 = 0.09 and R^2 = 0.1, respectively), although that finding is also analogous to those of Uldry & Fitting (R^2 = 0.09 and R^2 = 0.05, respectively) and of Kamide et al. (R^2 = 0.14 for males).[6,9] According to the ATS,[21] the wide variability in reference values is due to methodological differences that can influence the assessment of lung function, including the measurement technique, as well as individual, biological, and population aspects. In this context, we should highlight a number of differences between the present study and those conducted by Uldry & Fitting[6] and Kamide et al.[9] Our investigation adhered to the recommendations of the ATS[21] and was based on methodologies of earlier studies designed to obtain reference equations for lung function[14,18] and muscle function.[6,11,19] Another factor to consider is that there can be ethnic and individual differences within a given population. In comparison with the populations of European countries and of Japan, the Brazilian population is ethnically heterogeneous. Reference values should be based on recent data, and the most recent predictive equations for SNIP were published in 1995 and 2009.[6,9] Sociodemographic and environmental changes likely influence the results, which should therefore be updated periodically. As such, the differences observed might be attributed to differences in technical assessment, equipment, and population characteristics.

Although the present study has several strengths, certain limitations must be addressed. First, SNIP values were based on unmonitored FRC. However, this was understood as being at the end of a normal expiration, as reported in other studies, and determining FRC would make the SNIP technique expensive and inaccessible. Another potential limitation is that we did not include individuals over 80 years of age, and, consequently, the predictive equations proposed would not be valid for use in subjects who are over that age.

On the basis of the mean values obtained in our study sample, we have devised predictive equations for SNIP in the Brazilian population. These equations can be used in the diagnostic evaluation of Brazilians between 20 and 80 years of age.

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