Egyptian Journal of Chest Diseases and Tuberculosis (2014) **63**, 705–715

The Egyptian Society of Chest Diseases and Tuberculosis

Egyptian Journal of Chest Diseases and Tuberculosis

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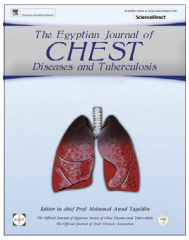

ORIGINAL ARTICLE

Reference values of capillary blood volume and pulmonary membrane diffusing capacity in North African boys aged 8 to 16 years

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Received 6 February 2014; accepted 17 February 2014
Available online 29 March 2014

KEYWORDS

Reference values;
Capillary blood volume;
Pulmonary membrane diffusing capacity;
Children

Abstract Lung diffusing capacity estimated using nitric oxide (NO) as the tracer gas has been proposed as a direct measure of the pulmonary membrane diffusing capacity for NO (Dm) and the pulmonary capillary blood volume (Vc). Thus, the aims of this study were to identify the factors influencing Vc and Dm and to establish linear regression equations for predicting reference values for Vc and Dm in healthy Tunisian boys aged 8 to 16 years.

Methods: It is a cross-sectional analytical study. The sample is formed of healthy Tunisian children aged 8 to 16 years. First, subjects responded to a questionnaire. Anthropometric and spirometric data were collected. DLNO and DLCO were measured and Dm and Vc were calculated simultaneously during a single breath maneuver using the double transfer technique for NO/CO. Statistical analyses were carried out using Statistica (Statistica Kernel version 6, StatSoft, 26 France). Significance was set at the 0.05 level.

Abbreviations: ATS, American Thoracic Society; BMI, body mass index; BSA, body surface area; BTPS, body temperature and pressure saturated; CO, carbon monoxide; DL, lung diffusing capacity; DLCO, lung diffusing capacity for carbon monoxide; DLNO, lung diffusing capacity for nitric oxide; Dm, pulmonary membrane diffusing capacity; DmCO, pulmonary membrane diffusing capacity for CO; DmNO, pulmonary membrane diffusing capacity for nitric oxide; ERS, European Respiratory Society; FEV_1, forced expiratory volume at the first second; FIO_2, fraction of inspired oxygen; FVC, forced vital capacity; GAP, Global Academic Programs; Hb, hemoglobin; He, helium; IC, confidence limits; ISSAC, International Study of Asthma and Allergies in Childhood; KCO, DLCO/VA; LLN, lower limit of normal; MMEF, maximum mid expiratory flow; N_2, nitrogen; NO, nitric oxide; NO_2, nitrogen dioxide; O_2, oxygen; PIO_2, the inspiratory pressure of oxygen; ppm, parts per million; RSD, residual standard deviation; RV, residual volume; SD, standard deviation; SEL, socioeconomic level; ULN, the upper limit of normal; VA, alveolar volume; Vc, pulmonary capillary blood volume

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Peer review under responsibility of The Egyptian Society of Chest Diseases and Tuberculosis.

Production and hosting by Elsevier

 http://dx.doi.org/10.1016/j.ejcdt.2014.02.007

Results: Eighty five boys were included to establish Vc and Dm reference values. Correlations between the Vc or Dm of the 85 healthy boys and anthropometric data showed that only BMI was not significantly correlated with Dm. The proposed Vc reference equation is: Vc (ml) = 11.3859 × age + 3.4613 × BMI − 117.0508. This model explains 45.7% of Vc variability. The proposed Dm reference equation is as follows: Dm (ml/min/mmHg) = 0.6430 × height − 41.5854. This model explains only 16.31% of Dm variability.

Conclusion: We have established a reliable and an available reference equation to interpret the results of Dm and Vc in healthy North African boys aged 8 to 16 years.

Introduction

The measurement of gas transfer in the lung is one of the few tests aimed at investigating deep lung function. According to the classic model of pulmonary diffusion proposed by Roughton and Forster [1] lung diffusing capacity (DL) for carbon monoxide (DLCO) is composed of two resistances arranged in series:

$$1/\mathrm{DLCO} = (1/\mathrm{Dm}) + (1/\Theta\mathrm{CO}^{*}\mathrm{Vc}) \quad (1)$$

where pulmonary membrane diffusing capacity (Dm) for CO (DmCO) is the CO conductance across the alveolar-capillary tissue membrane and plasma barrier; ΘCO is the rate of CO uptaken by the whole blood and combination with hemoglobin (Hb) measured in vitro, and Vc is the pulmonary capillary blood volume. In normal subjects, resistance of the membrane (1/DmCO) and erythrocytes [1/(ΘCO*Vc)] contribute almost equally to the overall diffusive resistance across the lung.

Lung diffusing capacity estimated using nitric oxide (NO) as the tracer gas (DLNO) has been proposed as a direct measure of the conductance of alveolar membrane (pulmonary membrane diffusing capacity for NO [Dm]) [2]. Because the reaction rate of NO binding to Hb is some 280 times faster than that of CO [3], the rate of NO uptaken by blood (ΘNO) is extremely large and 1/(ΘNO*Vc) becomes negligible, i.e. DLNO is approximately equal to Dm [2,3]. So the nitric oxide diffusing capacity (DLNO) reflects the properties of the alveolo-capillary membrane better than the DLCO [2]. Therefore DLNO can be defined as the true alveolo-capillary membrane diffusing capacity [3]. This non-invasive technique, easy to perform and repeat, could be of value in the diagnosis of many diseases. However the DLNO has been investigated by a small group of researchers, and is still not implemented in clinical routine.

Several childhood diseases can be explained (pathophysiology) and explored by the measure of diffusing capacity, Vc and DmNO, for example: Cystic fibrosis [4], childhood systemic diseases such as systemic lupus erythematosus [5], β-thalassemia [6] and childhood cancer [7]. These parameters can accurately locate the place of the anomaly: pulmonary capillary or alveolar membrane. This non-invasive technique may be useful in diagnosis, and during the follow-up of the disease as an early indicator of reactivation. Indeed, several childhood diseases are accompanied by a change in Vc and/or Dm and interpretation of these changes requires the knowledge of their normal values. In other words, we must have some ideas of physiological variations and reference values of these parameters in order to properly interpret pathological changes. Regarding children, to our knowledge, no studies have been made to determine the predicted values for lung diffusing capacity in healthy children.

Thus, we propose to study, for the first time, lung capillary blood volume and alveolar membrane diffusing capacity, using the NO–CO method, in healthy North African boys. The aims of this study are to: (1) identify the factors influencing Vc and DmNO in healthy North African boys aged 8 to 16 years. (2) Establish linear regression equations for predicting reference values for Vc and Dm in healthy North African boys aged 8 to 16 years.

Material and methods

Study design

This is a cross-sectional analytical study spread over eight months. It was conducted in the Department of Physiology and Functional Explorations in the Public Health Institution, Farhat HACHED Sousse (Tunisia) (altitude < 100 m). Study design consists of a sample of healthy Tunisian children in the region of Sousse, aged 8 to 16 years. Subjects were recruited from the children of the hospital workers, and from public and private schools. Information letters, clarifying the aims of the study, were put up in the Medicine Faculty and in different schools. When a subject was interesting, an appointment for distributing a medical questionnaire and exploration was fixed. Data from each volunteer child included: gender, age, height, weight, birth height and weight, smoking history (child or parents), medication use, medical history, physical examination and pulmonary capillary blood volume data. All children received a copy of their exploration and when an unknown dysfunction was discovered, they were sent to a specialist. Study approval was obtained from the Ethics committee of the Farhat Hached Public Institution of Health and written informed consent was obtained from all children and their parents.

Sample size

A large number of subjects (i.e., $n > 100$) are needed to ensure no significant difference between the published reference equations and those from the local community [8]. Therefore, to determine the influencing factors and establish a reference equation or normal values, we recruited an initial group of 172 children.

Subjects

Volunteer healthy children aged from 8 to 16 years were included. The following non-inclusion criteria were applied: chronic illnesses; history of pulmonary diseases or related