Rev Port Pneumol. 2017;xxx(xx):xxx–xxx

revista portuguesa de PNEUMOLOGIA
portuguese journal of pulmonology
www.revportpneumol.org

ORIGINAL ARTICLE

Hematological evaluation in males with obstructive sleep apnea before and after positive airway pressure

A. Feliciano[a,b,*], R. Linhas[c], R. Marçôa[c], A. Cysneiros[a], C. Martinho[d], R.P. Reis[e,b], D. Penque[f], P. Pinto[g,h,i], C. Bárbara[d,h,i]

[a] *Pneumology in Thorax Department, Centro Hospitalar Lisboa Norte, Lisboa, Portugal*
[b] *Faculdade de Ciências Médicas da Universidade Nova de Lisboa, Lisboa, Portugal*
[c] *Pneumology in Serviço de Pneumologia, Centro Hospitalar de Vila Nova de Gaia, Vila Nova de Gaia, Portugal*
[d] *Thorax Department, Centro Hospitalar Lisboa Norte, Lisboa, Portugal*
[e] *Cardiology Unit in Hospital Pulido Valente, Centro Hospitalar Lisboa Norte, Lisboa, Portugal*
[f] *Departamento de Genética Humana, Instituto Nacional de Saúde Dr. Ricardo Jorge, Lisboa, Portugal*
[g] *Sleep and Non Invasive Ventilation Unit in Thorax Department, Centro Hospitalar Lisboa Norte, Lisboa, Portugal*
[h] *Faculdade de Medicina da Universidade de Lisboa, Lisboa, Portugal*
[i] *ISAMB-Instituto de Saúde Ambiental, Faculdade de Medicina da Universidade de Lisboa, Lisboa, Portugal*

Received 17 July 2016; accepted 27 December 2016

KEYWORDS
RDW;
MPV;
PDW;
Red cell parameters;
Platelet parameters;
OSAS;
PAP

Abstract Obstructive sleep apnea syndrome (OSAS) is a systemic inflammatory disease associated with cardiovascular consequences. Red blood cell distribution width (RDW), mean platelet volume (MPV), and platelet distribution width (PDW) are recognized biomarkers of cardiovascular morbidity/mortality. Limited data is available on the association between these parameters and OSAS severity and the relationship with positive airway pressure therapy (PAP). In this prospective study of male OSAS patients we analyzed hematological data in order to evaluate their value in predicting OSAS severity, the relationship with sleep parameters, and their behavior under PAP. Seventy-three patients were included (mean age 46.5 years), of which 36 were mild (49.3%), 10 moderate (13.7%), and 27 severe (37%). The mean RDW increased significantly with OSAS severity and showed a positive correlation with respiratory disturbance index and hypoxemic burdens. Additionally, a group of 48 patients (mean age 47.2 years) were submitted to PAP. After six months, red blood cell count, hemoglobin, hematocrit, and platelet count showed a significant decrease ($p < 0.0001$; $p < 0.0001$; $p = 0.001$; $p < 0.0001$; respectively). Concerning OSAS severity, these parameters also significantly decreased in mild patients ($p = 0.003$; $p = 0.043$; $p = 0.020$; $p = 0.014$; respectively) but only hemoglobin, hematocrit, and platelet count decreased in severe cases ($p < 0.0001$; $p = 0.008$; $p = 0.018$; respectively). This study

* Corresponding author.
E-mail address: amelia.feliciano@chln.min-saude.pt (A. Feliciano).

http://dx.doi.org/10.1016/j.rppnen.2016.12.001

Please cite this article in press as: Feliciano A, et al. Rev Port Pneumol. 2017. http://dx.doi.org/10.1016/j.rppnen.2016.12.001

demonstrated an association between RDW values and OSAS severity. Moreover, red cell and platelet parameters changed significantly after PAP, supporting its cardiovascular protective effect. RDW may become a simple/inexpensive blood biomarker, making it useful in prioritizing OSAS patients waiting for polysomnography, and red cell and platelet parameters could be useful in PAP follow up.

Introduction

Obstructive sleep apnea syndrome (OSAS) is characterized by recurrent obstructive events and intermittent hypoxia, which in turn contributes to the systemic inflammation that underlies this disease and its consequences.[1–3] In concrete terms, the inflammation leads to endothelial dysfunction, which contributes to the pathogenesis of cardiovascular complications in OSAS, in addition to the exposure to risk factors, such as male gender, older age, obesity, and lack of exercise.[4]

Some red blood cells (RBC) and platelets indices have emerged as inflammatory biomarkers in various diseases, namely chronic obstructive pulmonary disease.[5] RBC distribution width (RDW) is a laboratory measure of size variability and respective heterogeneity of circulating erythrocytes. This parameter is calculated by division of standard deviation of RBC volume by mean corpuscular volume (MCV)[6] and is widely used to identify potential causes of anemia. In addition, increased RDW contributes to platelet activation. It may affect the outcomes in chronically ill patients as a strong predictor of all-cause mortality in population cohorts.[7,8] Hematocrit is expressed as the percent of a blood sample occupied by intact RBC, playing an important role in blood coagulability as it affects blood viscosity and platelet aggregation. Platelet size, as measured by mean platelet volume (MPV), is the best known of the platelet indices and has been a marker of platelet activity and aggregation. Increased MPV may reflect either increased platelet activation or increased numbers of large, hyper-aggregated platelets,[9] and may represent a link between hypercoagulability and inflammation.[10] Another marker of platelet activation is the platelet distribution width (PDW)[11] and is derived from direct flow cytometric measurements of platelet cell volume.

To understand OSAS pathophysiology better, a number of studies have recently appeared evaluating the behavior of hematological parameters, specifically RDW, MPV, and PDW, in this disease. However the information on the association between red cell[12–16] and platelets[12,15,17–21] indices and OSAS severity is controversial. Therefore, the aim of this study was to investigate the hematological parameters in OSAS, to assess their correlation with the disease severity, and their response to PAP therapy.

Material and methods

This prospective study consisted of 103 consecutive male subjects with suspected OSAS, who were evaluated through interviews at a Sleep Clinic.

Exclusion criteria were female gender (to avoid hormonal influence), other sleep disorders, chronic disorders such as anemia, polycythemia, other hematological diseases, hepatic, kidney, and neuromuscular disease. Also excluded were patients with heart failure, neoplasia, acute disease, hypoxemia, and previous PAP treatment.

Demographic and clinical data were collected in all selected patients. Additionally, these patients underwent an overnight polysomnography (PSG) study using Embla S7000 System (Embla; USA) with continuous sleep-technician monitoring. Sleep recordings and events were analyzed manually according to standard criteria.[22] The respiratory disturbance index (RDI), oxygen desaturation index (ODI), percentage of time with saturation under 90% (T90) and lowest oxygen saturation (SpO_2) were calculated.

Based on the RDI $\geq$ 5 events/hour, patients were diagnosed as OSAS (n = 73) and grouped into mild (RDI 5–14.9), moderate (RDI 15–29.9), and severe (RDI $\geq$ 30). Further, in pretreatment analysis of 73 patients, moderate and severe groups were combined (RDI $\geq$ 15).

After diagnosis, PAP therapy with automatic devices (S9, Resmed, Australia) was prescribed for 48 patients according to clinical and polysomnographic criteria,[23] in severe disease or in disease of any severity when associated with excessive diurnal sleepiness and/or cardio/cerebrovascular complications. Further, in pre/post treatment analysis of 48 patients, moderate and severe groups were combined (RDI $\geq$ 15).

Venous blood samples were collected during the morning after PSG (between 7:30 am and 09:00 am) and a 12 h fasting, into EDTA-coated polypropylene tubes. From patients who had undergone PAP treatment, and were free of any acute disease, a second morning blood sample was collected after six months under the same conditions as above described. In all samples, the collected blood was processed between one and two hours in the same equipment (ADVIA 2120i – Siemens). From routine complete hemogram, RBC count, hemoglobin, hematrocrit, MCV, RDW, platelets count, MPV, and PDW were determined.

At six months, patients under PAP were evaluated for compliance based on PAP software data. More than 4 h use/night for at least five days/week was accepted as compliance, as described previously.[24]

The study protocol was approved by the local ethics committees and all patients gave written informed consent.

Statistical analyses were performed using SPSS for windows software (SPSS Inc., Chicago, IL, USA). All variables were tested for normality of the distribution using Kolmogorov–Smirnov test. Continuous variables with normal distributions were expressed as mean ± standard deviation

Please cite this article in press as: Feliciano A, et al. Rev Port Pneumol. 2017. http://dx.doi.org/10.1016/j.rppnen.2016.12.001