Advs Exp. Medicine, Biology - Neuroscience and Respiration (2019) 43: 19–23
https://doi.org/10.1007/5584_2019_379

Published online: 3 May 2019

Chronic Obstructive Pulmonary Disease and Platelet Count

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Abstract

Recently, it has been shown in the murine model that platelet maturation takes place, to some extent, in the lungs. The extrapolation of these findings to humans leads to the possibility that chronic lung diseases could affect platelet maturation and, consequently, the platelet count. The aim of this study was to investigate whether there are changes in the platelet count in patients with chronic obstructive disease (COPD). The study included 44 patients, aged 66.5 ± 5.5 years, in stage II-IV COPD. The control group consisted of 48 age- and gender-matched patients without any respiratory diseases. We failed to find a significant difference in the platelet count between the two groups: 231 ± 80 *vs.* 223 ± 63 x 10^3/μL, respectively ($p = 0.61$). However, the number of platelets in the COPD patients was inversely associated with hemoglobin content ($r = -0.57$; $p < 0.001$), hematocrit ($r = -0.40$; $p = 0.006$), and the red cell count ($r = -0.51$; $p < 0.001$); the blood morphology indices that are typically increased in severe COPD. Such associations were absent in the control non-COPD group. We conclude that COPD has no influence on the platelet count in humans.

Keywords

Bone marrow · Chronic obstructive pulmonary disease · Hematopoiesis · Megakaryocytes · Platelets · Thrombogenesis

1 Introduction

Chronic obstructive pulmonary disease (COPD) is estimated to become the third leading cause of death worldwide by 2020 (Vogelmeier et al. 2017). In Poland, COPD was recognised as the main cause of death in 8024 patients in 2009. This number might be significantly underestimated as COPD is often accompanied by chronic cardiovascular diseases and lung cancer, which are recognized as the main reason of death instead (Sliwinski et al. 2014; Young et al. 2007).

COPD is frequently associated with polycythemia, increased hemoglobin concentration, and hypercoagulability, especially in patients with chronic respiratory failure (Sliwinski et al. 2014). The implication of lung destruction in the course of COPD on platelets' function and number is unclear. Recently, a study

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of Lefrançais et al. (2017), performed in a murine model of COPD, has shown that lungs may serve as a local reservoir for megakaryocytes and hematopoietic progenitor cells, in which almost one half of thrombocyte may be produced. That finding sheds new light on thrombopoiesis in mammals and raises a question of whether pulmonary thrombocyte production takes place in human lungs as well. If it were so, chronic pulmonary diseases, leading to lung tissue could affect the platelet count. Confirming this theory would have an important bearing on the anticoagulant treatment in thrombocytopenia, chronic lung and cardiovascular diseases, lung cancer treatment (Wang et al. 2018). Therefore, this study seeks to define the influence of advanced COPD stage on the platelet count in peripheral blood.

2 Methods

The study was conducted as a retrospective analysis. Patients were included in the analysis on the basis of a review of past medical files of the Department of Pneumology, Department of Internal Medicine, Autoimmune and Metabolic Diseases, and Department of Internal Medicine and Clinical Pharmacology of the Clinical Center of the Silesia Medical University in Katowice, Poland.

The study group consisted of 44 COPD patients, aged 66 ± 5.55 years, in stage II-IV of COPD diagnosed according the Polish Respiratory Society guidelines (Sliwinski et al. 2014). The control group consisted of 48 age- and gender-matched patients who were known to have no respiratory disease (Table 1). Low-dose acetylsalicylic acid (150 mg daily) was used by patients of both groups as antiplatelet prophylactic in coronary ischemic disease and the use of the drug was uninterrupted during the study time due to ethical reasons. Exclusion criteria were age >70 years and disorders that might affect the platelet count, such as diabetes, cancer (Lin et al. 2014; Habets et al. 2013), kidney failure (Dorgalaleh et al. 2013), chronic liver disease (Mitchell et al. 2016; Afdhal et al. 2008), and autoimmune diseases (Habets et al. 2013; Cines et al. 2009). Patients admitted to the hospital in the acute condition, with inflammatory diseases, or exacerbations of chronic disease, as well as current cigarette smokers were also excluded from the study.

Continuous variables were expressed as means ±SD. The Shapiro-Wilk test was used to evaluate the distribution pattern of data. Statistical differences between the COPD and control groups were evaluated with the Student *t*-test or the Mann–Whitney U test. Differences in the qualitative variables were evaluated with a Chi-squared test. Pearson's correlation coefficient was used to evaluate correlations when both variables were normally distributed. Otherwise, Spearman's rank correlation coefficient was used. A p-values <0.05 defined statistically significant differences. A commercial of statistical v13.1 package was used for statistical elaboration (StatSoft; Tulsa, OK).

3 Results

The results of complete blood counts are displayed in Table 2. The numbers of red and white blood cells were significantly greater in COPD than those in the control group ($p = 0.003$ and $p = 0.045$, respectively). Hematocrit and hemoglobin concentration were higher in the COPD group as well ($p = 0.0001$ and $p = 0.030$, respectively). The mean corpuscular hemoglobin concentration was higher in the control group ($p = 0.00001$). There were no appreciable differences in the platelet counts between the two groups.

Table 1 Study patients

	COPD group *(n = 44)*	Control group *(n = 48)*	p-value
Gender (F/M)	14/30	16/32	0.88
Age (min-max) (years)	61.5 ± 5.5 (51–70)	62.2 ± 6.6 (34–70)	0.39

Table 2 Complete blood counts in the COPD and control groups

Parameter	COPD group *(n = 44)*	Control group *(n = 48)*	p-value
HCT (%)	44.5 ± 4.1	41.3 ± 3.3	0.0001
HB (g/dL)	14.7 ± 1.4	14.1 ± 1.2	0.030
RBC (10^6/uL)	4.9 ± 0.5	4.6 ± 0.4	0.003
WBC (10^3/uL)	8.1 ± 2.2	7.2 ± 2.1	0.045
PLT (10^3/uL)	231.0 ± 80.5	223.0 ± 63.0	0.610
MCV (fL)	91.9 ± 5.5	90.8 ± 4.7	0.290
MCH (pg)	30.2 ± 2.5	30.9 ± 1.7	0.150
MCHC (g/dL)	32.9 ± 1.4	34.0 ± 0.9	0.00001

Data are means ±SD
HCT hematocrit, *HB* hemoglobin, *RBC* red blood cell, *WBC* white blood cell, *PLT* platelets, *MCV* mean cell volume, *MCH* mean cell hemoglobin, *MCHC* mean corpuscular hemoglobin concentration

Table 3 Associations between the platelet count and other blood morphology prameters in the COPD and control groups

	Study Group *(n = 44)*		Control group *(n = 48)*	
Parameter	*r*	p-value	*r*	p-value
PLT – HB	−0.57	<0.001	0.12	0.400
PLT – RBC	−0.40	0.006	−0.02	0.880
PLT – WBC	0.37	0.010	0.39	0.006
PLT – HCT	−0.51	<0.001	−0.15	0.290

PLT platelets, *HB* hemoglobin, *RBC* red blood cell, *HCT* hematocrit, *WBC* white blood cell

Table 3 displays significant associations between the number of platelets and parameters of blood morphology. In both COPD and control groups, there was a positive association between the number of platelets and leukocytes. In the COPD group only, there was an adverse association between the number of platelets, on the one side, and that of erythrocytes and the values of hemoglobin and hematocrit, on the other side. That led us to the assumption that COPD might affect thrombopoiesis in the advanced stages of COPD. We the performed a secondary analysis dividing the COPD group into the subgroups consisting of normocythemia, polycythemia, and anemia. That analysis, however, failed to substantiate the presence of any appreciable differences in the number of platelets depending on the COPD-induced disturbances in blood morphology.

4 Discussion

Recent experimental studies have shown that thrombocyte maturation may take place in the lung tissue, aside from hematologic tissues (Lefrançais et al. 2017). In the murine model, those authors have shown that the lungs are a reservoir of hematopoietic progenitor cells and the site of platelet formation. In view of this biological plausibility, the present study was undertaken to address the issue of whether lung disease could have an impact on the number of platelets in peripheral blood. We chose a group of COPD, having a sever course of the disease, as evidenced by enhanced levels of erythrocytes, hemoglobin, and hematocrit. We found an adverse association between the number of platelets and the levels of blood parameters above outlined, typically enhanced in COPD; the phenomenon was absent in the control group. That finding indeed suggested that COPD, particularly its severe course, might affect the number of platelets. Nonetheless, further insight into the data failed to substantiate the presence of any appreciable differences in the number of platelets, depending on the severity of abnormalities in COPD blood morphology such as anemia or polycythemia. Further, we failed to substantiate the presence of any

appreciable differences in the number of platelets between the COPD and non-COPD patients. Therefore, lung tissue damage, at least in the COPD condition, is unlikely to lead to clinically important thrombocytopenia and thrombocytopenia-related bleeding complication.

For years, scientists have been trying to determine the possible locations of platelets formation in the body (Howell and Donahue 1937). The lungs as a potential location of platelet formation has originally suggested by Levine et al. (1993) on the basis of a much larger number of megakaryocytes found in the blood reaching the lungs than leaving them. A microscopic examination has confirmed the maturity and proper morphology of megakaryocytes in that study.

In another study, cigarette smokers have been stratified into COPD and non-COPD patients. It has been shown that platelet count is higher in the COPD patients (Cakmak et al. 2009). The nature of changes in the platelet count in COPD patients remains unsettled, but apparently the smoking habit might be somehow involved. Smoking in COPD increases the toxic burden on the lung tissue, which should rather lead to a decrease in the platelet count if the lung participated in thrombocyte maturation. In that study, exclusion criteria included the chest, abdominal and ocular surgery in the preceding 3 months, and rheumatologic, hematologic, and infectious diseases. In contrast, in the present study we added other disorders that could affect platelet production, when being an accompaniment to COPD, such as diabetes, cancer, chronic kidney and liver diseases, and autoimmune diseases, which could explain divergent results.

In the present study, patients in both COPD and control groups were treated acetylsalicylic acid (ASA). Smoking is a risk factor not only for COPD but also for ischemic heart disease, either developing more frequently in the elderly. The drug was used as prophylaxis against exacerbations ischemic heart disease, and its use could not be interrupted due to ethical reasons. ASA has antiplatelet activity. Since it was given to the patients of both groups in like manner, they were studied on a common background and any effect of ASA on plate function should be balanced off.

A major limitation of the study was its retrospective nature, which made it impossible to perform additional tests, for instance, lung testing. Also, there was only one patient with polycythemia in the COPD group. A wide availability of home oxygen therapy and noninvasive assisted ventilation cause that much fewer COPD patients are nowadays observed with polycythemia, compared to the past times. Yet COPD patients are still most often cigarettes smokers or ex-smokers and the effect of smoking on the platelet count should be taken into account. The issue is contentious and no hard evidence exists of the effect of smoking on the platelet count (Suwansakri et al. 2004; Erikssen et al. 1977). Therefore, the potential effect of cigarette smoking on the blood platelets was not considered in this study.

In conclusion, a prospective human study is required to settle the issue of an effect of COPD and other lung tissue damaging disorders on the platelet count. Firstly, however, unequivocal evidence is needed that the lung tissue does participate in the extra bone marrow formation or maturation of thrombocytes. Obtaining such evidence is likely bound to require studies involving megakaryocyte labeling in biopsied specimens of lung parenchyma. The issue of the lung-platelet link is, however, important as it has to do with the risk assessment of thrombocytopenia and blood clotting homeostasis in lung disorders, as well as with pulmonary alveolar and microvascular homeostasis and inflammation (Weyrich and Zimmerman 2013; Cakmak et al. 2009). For the time being we are left with no convincing indications of the potential impact of COPD-related lung damage on the platelet function and count.

Acknowledgments Funded by the Silesian Medical University grant KNW-1-052/N/7/K.

Conflicts of Interest The authors declare no conflicts of interest in relation to this article.

Ethical Approval This is a retrospective study based on a review of medical files. Therefore the article does not contain any studies with human participants performed by any of the authors.

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