Research Article

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Ophthalmic Changes in Patients with Chronic Obstructive Pulmonary Disease: Case-Control Study

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Abstract

Purpose: To evaluate the prevalence of ophthalmological changes in patients with Chronic Obstructive Pulmonary Disease (COPD) cared for at the Pneumology and Ophthalmology Departments at Medical School-Unifacisa-Campina Grande-Paraíba-Brazil.

Materials and Methods: Twenty-two smoker patients with COPD (study group) and 22 healthy controls that underwent routine ophthalmological examination (control group) were enrolled in the investigation. They were homogeneous regarding age, gender, presence of Systemic Arterial Hypertension (SAH) and Diabetes Mellitus (DM). They were examined for the presence of cataract and Age Related Macular Disease (AMD).

Results: The prevalence of ophthalmologic changes was significantly different in the two groups. Eight (36.4%) patients presented with cataract requiring surgical intervention, while one (4.5%) person in the control group had cataract ($p = 0.0212$). Regarding AMD, 10 (45.5%) smoker COPD patients had this disease, whereas in the control group, one (4.5%) person had this disease ($p = 0.0039$).

Conclusion: From the results one can conclude that there is strong association between smokers diagnosed with COPD with cataract and AMD patients, reinforcing the need for a protocol for referral of these patients to the ophthalmologist.

Keywords: Chronic obstructive pulmonary disease, Non communicable chronic disease, Smoking, Cataract, Age related macular disease

Introduction

Non-communicable Chronic Diseases (CNCDs) are considered a serious public health problem, and it is unlikely that Brazil will achieve the goals previously agreed upon with the World Health Organization and the United Nations to curb NCDs and their risk factors [1-3]. Among the CNCDs of epidemiological importance, Chronic Respiratory Diseases, such as Chronic Obstructive Pulmonary Disease (COPD), are considered a global public health problem [4,5], accounting for

approximately 1.6 million, only due to air pollution [6]. The mortality in patients with COPD and coexisting heart failure was strongly associated with age, male sex and other comorbidities. Of those three predictors, only other comorbidities can be influenced. Heart failure and other comorbidities should be recognized early and properly treated in order to improve survival in patients with coexisting COPD and heart failure [7,8].

COPD is characterized as a preventable disease with some significant extra pulmonary effects, associated with

persistent, progressive, and not totally reversible airflow limitation [9-11]. According to the Global Initiative for Chronic Obstructive Pulmonary Disease (GOLD, 2006), the spirometric diagnostic criteria for this disease is the ratio of forced expiratory volume in the first second / forced vital capacity (FEV1 / FVC) of less than 0.7 after the bronchodilator and, depending on the degree of bronchial obstruction, patients were classified into four groups according to established spirometric criteria [12]. Therefore, different groups of COPD patients have systemic manifestations that may compromise functional capacity and cognitive behavior more severely than others and thus reduce quality of life and increase mortality among these individuals [13]. Among the most well-known manifestations are heart diseases and pulmonary vascular diseases, as well as malnutrition with dysfunction of the skeletal muscles, osteoporosis, anemia, among others [14,15]. In this context, ocular complications are understood as unrecognized manifestations, although they may be potentially serious and, in many cases, irreversible if not recognized in a timely manner, such as hypertensive retinopathy, retinal hemorrhage, glaucoma, age-related macular degeneration, endothelial vulnerability to cataract surgery, changes in the nerve fiber layer, among others [16-21]. Hence, the importance of such disorders being investigated during the follow-up of these patients in clinical practice, alerting health professionals about their existence and severity, since the knowledge about systemic diseases evolving with ocular complications [22,23] is scarce among the professionals of the eye health area.

The purpose of this research was to evaluate the ophthalmological alterations in patients with COPD treated at the Department of Pulmonology of the Medical School- Unifacisa-Campina Grande-Paraíba and to compare them with the control group constituted by elderly individuals who were not sick and non-smokers. In addition, it hopes to identify the level of knowledge of COPD patients and the control group regarding the possibility of ophthalmological changes induced by this disease.

Materials and Methods

The research was performed at the Departments of Pulmonology and Ophthalmology from the Medical School- Unifacisa-Campina Grande-Paraíba, where the full clinical and ophthalmological examination of all participants were carried out in 2017. A case-control, clinical, prospective, cross-sectional, observational and analytical study was developed. In the case group,

22 smoker patients with COPD followed up at the Department of Pulmonology confirmed by spirometry and chest imaging. The control group enrolled 22 healthy, non-smokers people cared for at the Ophthalmology Department for routine vision check-up.

Patients with pulmonary infectious diseases, carriers of lung carcinomas, hemoglobinopathies and individuals who were taking anticoagulants were excluded from the study.

In the Department of Ophthalmology, anamnesis data were obtained (age, sex, signs and symptoms present at the moment of care); Personal history of previous eye treatment, such as: use of glasses and / or contact lenses, eye drops, previous eye surgery, laser treatment; Other systemic diseases, such as: Systemic Arterial Hypertension (SAH), Diabetes Mellitus (DM), Obesity; Family history (cases of strabismus, glaucoma, blindness, retinal detachment); Exam of Visual acuity from Far (5 meters) and close (33 cm) using the table of Snellen and Jeager, respectively. Visual acuity from far (AVL) was defined as normal at or better than 20/40 and abnormal acuity worse than 20/40, for better statistical definition. Subsequently, the previous biomicroscopy examination was performed, using the Topcon Slit Lamp. Then, the tonometry was performed with the aid of the Optlaza® and the retinal mapping examination under mydriasis with the aid of the Eyotec Binocular Indirect Binocular Ophthalmoscope®.

All data were recorded in an electronic medical database, and all participants were examined by the same resident and an advisory staff, retina specialist at Medical School- Unifacisa.

At the end of the care, a questionnaire was directed to study participants about the knowledge of possible associations of COPD and an ocular disease, whose answers was categorized as: Group 0: without knowledge, group 1: with partial knowledge and group 2: with knowledge.

Qualitative variables were expressed by absolute and relative frequencies. Chi-square tests, Fisher's exact test and the Fisher-Freeman-Halton tests were used to verify the association between the qualitative variables. The quantitative variables were expressed by mean and standard deviations. The non-parametric Mann-Whitney test was used to compare differences among the means. To verify normality, the Shapiro-Wilk test was used. The

significance level adopted was 5%, so if the p-value is equal to or less than the level of significance when the null hypothesis was rejected.

Results

Forty four individuals (22 in the case group and 22 in the control group) were enrolled in the investigation, and the 88 eyes were analyzed. Three eyes were excluded due to the impossibility of evaluating all of the ophthalmological variables, such as vascular emergency, retina and optic nerve, among others.

In table 1, one can observe the data regarding the age and gender characteristics of the individuals in the sample, as well as the personal history of having or not Diabetes Mellitus (DM) and Systemic Hypertension (SAH), as well as the habit of active or passive smoking.

In table 2, one can see the results of the complete ophthalmic examination. It can be observed that the parameters of the variables tonometry, crystalline, arterial and venous vessels and retina are associated with the presence or not of COPD and smoking.

In table 3, one can observe that the variables cataract and ARMD were more frequent in the case group. As a consequence there is strong indication that the variables COPD and smoking are associated with the presence of cataract and ARMD.

In table 4, relation to the case group, 11 (50%) of the patients had been diagnosed and followed up with a pulmonologist for less than 12 months, while seven (31.8%) had COPD. They had been diagnosed between 13 months to five years and the others, four (19%), had been diagnosed for more than five years.

Regarding the result on the COPD questionnaire, it can be observed that in the case group the majority of patients did not know how to clarify specific questions about the disease they suffer.

Discussion

This study is relevant given the evidence that ophthalmological manifestations in COPD patients are infrequently recognized and therefore are not part of the follow-up protocol for these patients [16-21,24]. The current research findings support the referral to the ophthalmologist of COPD patients followed in the routine of pulmonology.

The sample consisted of homogeneous groups in relation to gender, age, SAH and DM. This means that these anthropometric variables and comorbidities presented similar frequencies, as there is no difference between age means, as well as the frequencies of comorbidities. The most logical explanation is that these two chronic noncommunicable diseases (NCD) have age as an independent risk factor.

The higher frequency of cataracts among individuals with COPD in the present study may be explained by the indiscriminate use of corticosteroids in the course of treatment of these patients. In addition, other alterations may arise as a result of this indiscriminate use, such as: diabetes, osteoporosis, water retention, secondary infection and psychosis [24]. On the other hand, other studies show the well-established causality relationship between nuclear cataract and smoking, especially in those heavy smokers (from 40 to 60 cigarettes a day) [25]. Being an active heavy smoker greatly increases the risk of cataract and stopping smoking reduces the risk, but remains increased compared to those who never had smoked. The possible pathophysiology may be related to changes in the levels of metal ions that occur as a consequence of normal aging in many tissues [26], and this change is influenced by the act of smoking. However prevention can be done by healthy nutrition including high-dose zinc and antioxidant vitamin supplement [27].

Of the many environmental and modifiable factors related to ARMD, smoking is considered the most important. Smoking is associated with an increased risk of cataract, fact evidenced in the present study. There is consensus regarding the association between smoking and advanced AMD, that is, development of geographic atrophy and choroidal neovascularization. The pathophysiology is unknown, but it is believed that it may be directly related to oxidative stress induced by nicotine or indirectly due to the promotion of atherosclerosis, or due to its effect on the decrease in macular pigment density. Stop smoking, is associated with a reduction in the possibility of inducing cataract and ARMD, since the benefits of quitting smoking decrease both the chance of having choroidal neovascularization and that of having a geographical atrophy [28,29].

On the other hand, independently of the history of smoking, other factors such as respiratory symptoms, history of emphysema and involvement of lung function are associated with the risk of onset and even worsening of AMD [29], a fact evidenced in the results of the current

Table 1: Demographic characteristics, comorbidities and habit of life.

Variables		Grups		Total	p-Value
		Case	Control		
Sex	Female	16(72.7%)	14 (63.6%)	30 (68.2%)	0.517
	Male	6 (27.3%)	8 (36.4%)	14 (31.8%)	
Age	Average	65.4±8.0	68.4±7.2	-	0.378
Sah	No	10(45.5%)	14 (63.6%)	24 (54.5%)	0.226
	Yes	12(54.5%)	8 (36.4%)	20 (45.5%)	
DM	No	18(81.8%)	22 (100%)	40 (90.9%)	0.108
	Yes	4 (18.2%)	0 (0.0%)	4 (9.1%)	
Smokers	No	0 (0.0%)	21 (95.5%)	21 (47.7%)	<0.001
	Ex smoker	15(68.2%)	0 (0.0%)	15 (34.1%)	
	Passive smoker	1 (4.5%)	1 (4.5%)	2 (4.5%)	
	Heavy Active Smoker	6 (27.3%)	0 (0.0%)	6 (13.6%)	

Table 2: Results of ophthalmologic examination

Variables		Groups		Total	p-Value
		Study	Control		
Lens	Normal	19(43.2%)	16 (36.4%)	35 (39.8%)	<0.001
	Not Normal	14(31.8%)	28 (63.6%)	42 (47.7%)	
	Pseudophakia	11(25.0%)	0 (0.0%)	11 (12.5%)	
Arterial And Venous Vessels	Normal	13(31.7%)	26 (59.1%)	39 (45.9%)	0.011
	Not Normal	28(68.3%)	18 (40.9%)	46 (54.1%)	
Retina	Normal	19(46.3%)	42 (95.5%)	61 (71.8%)	<0.001
	Not Normal	22(53.7%)	2 (4.5%)	24 (28.2%)	
Tonometry	Average	17.42±3.4	14.34±4.7	-	<0.001

Table 3: Ophthalmic changes found in the sample.

Variables		Groups		Total	p-Value
		Study	Control		
Cataract	No	14(63.6%)	21 (95.5%)		0.021
	Yes	8 (36.4%)	1 (4.5%)		
ARMD	No	12(54.5%)	21 (95.5%)		0.004
Age-Related Macular Degeneration	Yes	10(45.5%)	1 (4.5%)		

Table 4: Results of knowledge of COPD.

Variables		Grups		Total	P-Value
		Case	Control		
COPD Questionnaire	No knowledge	19(86.4%)	8 (36.4%)	27 (61.4%)	0.002
	Partial Knowledge	2 (9.1%)	11 (50.0%)	13 (29.5%)	
	Knowledge about the subject	1 (4.5%)	3 (13.6%)	4 (9.1%)	

study.

A constant supply of oxygen is crucial for the maintenance of homeostasis in the body, especially in tissues with high demand for oxygen, as is the case with the retina. It is well established that patients with severe COPD (Stage 3) present changes in retro bulbar hemodynamics and that hypoxemia and hypercapnia can cause vasodilation of arterioles, venules and capillaries, as well as increase the permeability of their walls, inducing clinically evident changes in the retina [16,17]. In the present study, 15 patients (68.2%) of the case group presented alterations in arterial and venous vessels, such as: vascular attenuation, vascular tortuosity, rectification of arterial vessels and presence of pathological arteriovenous junctions, suggesting hypertensive retinopathy probably due to COPD and smoking.

A higher mean intraocular pressure (IOP) was also significantly observed in the case group, which maintained a mean IOP of 17.42 mmHg ($\pm$ 3.4) compared to the control group with mean IOP of 14.34 mmHg ($\pm$ 4.7). It is already known that smoking is associated with the immediate increase of IOP by vasoconstriction, which determines the increase of pressure in the episcleral veins and, consequently, the reduction of the outflow of the aqueous humor and the increase of the IOP, being, therefore, an important factor of risk for the development of glaucoma [30].

Regarding the result on the COPD questionnaire, it was observed that 86.4% of the patients in the case group did not know how to clarify specific questions about the disease suffered. An alarming result that serves as a guide to the professionals who take care of such patients. It is necessary to improve the patient doctor communication, improving the explanation with accessible language, including the definition of this pulmonary disorder and how it may imply in the health of the organism, especially in the eye function.

The limitations of this study include a small sample that was neither probabilistic nor randomized. However, it represents the basis for further investigation on the effect of COPD and smoking on the retina blood supply.

Conclusion

It was observed association between COPD and smoking with the presence of cataract, AMD, alteration of arterial and venous retinal vessels, as well as an increase in the mean IOP measurement, reinforcing the

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need for a referral protocol for these patients to the ophthalmologist.

References

1. Allen L, Williams J, Townsend N, et al. Socioeconomic status and non-communicable disease behavioural risk factors in low-income and lower-middle-income countries: a systematic review. *The Lancet Global Health*. 2017;5(3):e277-e289. doi: [http://dx.doi.org/10.1016/S2214-109X\(17\)30058-X](http://dx.doi.org/10.1016/S2214-109X(17)30058-X)
2. Sommer I, Griebler U, Mahlknecht P, et al. Socioeconomic inequalities in non-communicable diseases and their risk factors: an overview of systematic reviews. *BMC Public Health*. 2015;15(1). doi: <http://dx.doi.org/10.1186/s12889-015-2227-y>
3. Malta DC, Duncan BB, Barros MB de A, et al. Medidas de austeridade fiscal comprometem metas de controle de doenças não transmissíveis no Brasil. *Ciência & Saúde Coletiva*. 2018;23(10):3115-3122. doi: <http://dx.doi.org/10.1590/1413-812320182310.25222018>
4. Hatipoglu U. Chronic obstructive pulmonary disease: More than meets the eye. *Annals of Thoracic Medicine*. 2018;13(1):1. doi: http://dx.doi.org/10.4103/atm.ATM_193_17
5. Moore E, Chatzidiakou L, Kuku M-O, et al. Global Associations between Air Pollutants and Chronic Obstructive Pulmonary Disease Hospitalizations. A Systematic Review. *Ann Am Thorac Soc*. 2016;13(10):1814-1827. doi: <http://dx.doi.org/10.1513/AnnalsATS.201601-064OC>
6. Schraufnagel DE, Balmes JR, Cowl CT, et al. Air Pollution and Noncommunicable Diseases: A Review by the Forum of International Respiratory Societies' Environmental Committee, Part 2: Air Pollution and Organ Systems. *Chest*. November 2018. doi: <http://dx.doi.org/10.1016/j.chest.2018.10.041>
7. Kaszuba E, Odeberg H, Råstam L, Halling A. Impact of heart failure and other comorbidities on mortality in patients with chronic obstructive pulmonary disease: a register-based, prospective cohort study. *BMC Family Practice*. 2018;19(1). doi: <http://dx.doi.org/10.1186/s12875-018-0865-8>
8. Shafuddin E, Chang CL, Hancox RJ. Comparing severity scores in exacerbations of chronic obstructive pulmonary disease. *The Clinical Respiratory Journal*. 2018;12(12):2668-2675. doi: <http://dx.doi.org/10.1111/crj.12973>
9. Piotrowski W, Miłkowska-Dymanowska J, Zalewska-Janowska A, Górski P, Adam B. Underrecognized

- comorbidities of chronic obstructive pulmonary disease. *International Journal of Chronic Obstructive Pulmonary Disease*. July 2015;1331. doi: <http://dx.doi.org/10.2147/COPD.S82420>
10. Ozcimen M, Sakarya Y, Kurtipek E, et al. Peripapillary choroidal thickness in patients with chronic obstructive pulmonary disease. *Cutaneous and Ocular Toxicology*. 2016;35(1):26-30. doi: <http://dx.doi.org/10.3109/15569527.2015.1004079>
 11. Morgan BW, Grigsby MR, Siddharthan T, et al. Epidemiology and risk factors of asthma-chronic obstructive pulmonary disease overlap in low- and middle-income countries. *Journal of Allergy and Clinical Immunology*. October 2018. doi: <http://dx.doi.org/10.1016/j.jaci.2018.06.052>
 12. Jezler S, Holanda MA, José A, Franca S. Ventilação mecânica na doença pulmonar obstrutiva crônica (DPOC) descompensada. *Jornal Brasileiro de Pneumologia*. 2007;33(suppl 2):111-118. doi: <http://dx.doi.org/10.1590/S1806-37132007000800006>
 13. Heslop-Marshall K, Baker C, Carrick-Sen D, et al. Randomised controlled trial of cognitive behavioural therapy in COPD. *ERJ Open Research*. 2018;4(4):00094-2018. doi: <http://dx.doi.org/10.1183/23120541.00094-2018>
 14. Barnes PJ, Celli BR. Systemic manifestations and comorbidities of COPD. *European Respiratory Journal*. 2009;33(5):1165-1185. doi: <http://dx.doi.org/10.1183/09031936.00128008>
 15. Cavailles A, Brinchault-Rabin G, Dixmier A, et al. Comorbidities of COPD. *European Respiratory Review*. 2013;22(130):454-475. doi: <http://dx.doi.org/10.1183/09059180.00008612>
 16. Gok M, Ozer MA, Ozen S, Botan Yildirim B. The evaluation of retinal and choroidal structural changes by optical coherence tomography in patients with chronic obstructive pulmonary disease. *Current Eye Research*. 2018;43(1):116-121. doi: <http://dx.doi.org/10.1080/02713683.2017.1373824>
 17. Adžić-Zečević A, Milojko B, Janićijević-Petrović MA. Vascular changes in the retina in patients with chronic respiratory insufficiency. *Vojnosanit Pregl*. 2014;71(12):1132-1137.
 18. Ugurlu E, Pekel G, Altinisik G, Bozkurt K, Can I, Evyapan F. New aspect for systemic effects of COPD: eye findings. *The Clinical Respiratory Journal*. 2018;12(1):247-252. doi: <http://dx.doi.org/10.1111/crj.12523>
 19. Soler N, Romero-Aroca P, Gris O, Camps J, Fernandez-Cur Tre Ophthal, 2(1): 113-119 (2019)
 - Ballart J. Corneal endothelial changes in patients with chronic obstructive pulmonary disease and corneal vulnerability to cataract surgery. *J Cataract Refract Surg*. 2015;41(2):313-319. doi: <http://dx.doi.org/10.1016/j.jcrs.2014.04.043>
 20. Wittström E. Central Retinal Vein Occlusion in Younger Swedish Adults: Case Reports and Review of the Literature. *The Open Ophthalmology Journal*. 2017;11(1):89-102. doi: <http://dx.doi.org/10.2174/1874364101711010089>
 21. Shih KC, Lam KS-L, Tong L. A systematic review on the impact of diabetes mellitus on the ocular surface. *Nutrition & Diabetes*. 2017;7(3):e251-e251. doi: <http://dx.doi.org/10.1038/nutd.2017.4>
 22. Vaes AW, Spruit MA, Theunis J, et al. Looking into the eye of patients with chronic obstructive pulmonary disease: an opportunity for better microvascular profiling of these complex patients. *Acta Ophthalmologica*. 2018;96(6):539-549. doi: <http://dx.doi.org/10.1111/aos.13765>
 23. Jonas JB, Wei WB, Xu L, Wang YX. Systemic inflammation and eye diseases. The Beijing Eye Study. Liu G-S, ed. *PLOS ONE*. 2018;13(10):e0204263. doi: <http://dx.doi.org/10.1371/journal.pone.0204263>
 24. Langford-Smith A, Tilakaratna V, Lythgoe PR, Clark SJ, Bishop PN, Day AJ. Age and Smoking Related Changes in Metal Ion Levels in Human Lens: Implications for Cataract Formation. Al-Ghoul KJ, ed. *PLOS ONE*. 2016;11(1):e0147576. doi: <http://dx.doi.org/10.1371/journal.pone.0147576>
 25. Irie H, Chubachi S, Sato M, et al. Impact of cataract on health-related quality of life in a longitudinal Japanese chronic obstructive pulmonary cohort. *Chronic Respiratory Disease*. 2018;15(4):329-338. doi: <http://dx.doi.org/10.1177/1479972317745735>
 26. Langford-Smith A, Tilakaratna V, Lythgoe PR, Clark SJ, Bishop PN, Day AJ. Age and Smoking Related Changes in Metal Ion Levels in Human Lens: Implications for Cataract Formation. Al-Ghoul KJ, ed. *PLOS ONE*. 2016;11(1):e0147576. doi: <http://dx.doi.org/10.1371/journal.pone.0147576>
 27. Mitchell P, Liew G, Gopinath B, Wong TY. Age-related macular degeneration. *The Lancet*. 2018;392(10153):1147-1159. doi: [http://dx.doi.org/10.1016/S0140-6736\(18\)31550-2](http://dx.doi.org/10.1016/S0140-6736(18)31550-2)
 28. Anastasopoulos E, Haidich AB, Coleman AL, et al. Risk factors for Age-related Macular Degeneration in a Greek population: The Thessaloniki Eye Study. *Ophthalmic Epidemiology*. 2018;25(5-6):457-469. doi: <http://dx.doi.org/10.1016/j.ophidis.2018.05.003>

<http://dx.doi.org/10.1080/09286586.2018.1512634>

29. Armstrong RA, Mousavi M. Overview of Risk Factors for Age-Related Macular Degeneration (AMD). *J Stem Cells*. 2015;10(3):171-191.
30. Chiotoroiu S, Pop de Popa D, Ștefăniu G, Secureanu F, Purcărea V. The importance of alcohol abuse and smoking in the evolution of glaucoma disease. *J Med Life*. 2013;6(2):226-229.

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