COVID-19 and Smoking: Epidemiological, Biological, Psychosocial Aspects and Implications for the National Tobacco Control Policy

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Covid-19 y Tabaquismo: Aspectos Epidemiológicos, Biológicos, Psicosociales e Implicaciones para la Política Nacional de Control del Tabaco

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INTRODUCTION

According to the United Nations, the pandemic of the novel coronavirus (2019-nCoV) is the greatest challenge since the Second World War[1] for the humanity. The insufficient knowledge about its epidemiologic, biologic, psychosocial characteristics, forms of effective prevention and treatment mobilized an unprecedented global strategy running against the time, attempting to find solutions to mitigate the sanitary and socioeconomic impacts of this invisible enemy. One result of this learning addresses the identification of more vulnerable groups to transmission and health complications of the disease by coronavirus 2019 (coronavirus disease 2019 – COVID-19), among which, are the smokers who range nearly 1 billion individuals in the world and, in Brazil, more than 20 millions[2,3].

It is important to remind that in 1986, the 39th World Health Assembly recognized smoking as a pandemic[4]. Currently, this pandemic responds for 8 million annual deaths in the world and has a financial global toll of US$ 1.4 trillion annually for all nations[5,6]. In Brazil, it generates 157 thousand deaths annually and costs more than R$ 57 billion per year[7].

The objective of this article is to gather information about epidemiological, biological and psychosocial aspects between smoking and COVID-19, contributing to reflection on the potential of preventive measures and smoking reduction among the public policies against the novel coronavirus.

DEVELOPMENT

Does smoking increase the risk for COVID-19?

Evidences that smoking is associated to a higher chance of adverse outcomes in the novel coronavirus infection are growing. Among the infected patients, smokers have twice the risk of being hospitalized in intensive care units, needing mechanical ventilation and dying than non-smokers patients[8-13].

Smokers, when compared to non-smokers, have a significantly higher risk of developing chronic diseases, such as cancer, cardiovascular, chronic obstructive pulmonary disease and diabetes[14]. They also suffer with adverse effects of systemic character, such as the alteration of the immune system functioning, which explains the higher risk of bacterial and viral respiratory infections and greater risk of developing and dying of tuberculosis, when compared to non-smokers[14]. The majority of these conditions and tobacco-related diseases was identified as risk factor for COVID-19[15-20] complications.

Studies have demonstrated that the vapors produced by electronic and heated not burn cigarettes generate

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inflammatory and toxic effects in the lungs and cardiovascular systems of its users. The Unite States of America (USA), one of the countries where the use of electronic cigarettes among young adults has grown the most, has tackled an epidemic of severe cases of acute lung lesions, along with respiratory failure, due to the use of these products for vaping, known as EVALI (e-cigarette or vaping product use associate lung injury)[21-24]. Therefore, it is plausible that the use of electronic devices to smoke may contribute for an elevated risk of complications by COVID-19 among its users.

Some studies that identified the low prevalence of smokers among hospitalized patients with COVID-19, when compared with the prevalence of smokers in general population[25,26], were used to speculate about a possible protective role of smoking in the coronavirus infection[27-29]. These studies, challenged by several health entities, need to be interpreted cautiously, considering the similarity between physiopathological mechanisms of smoking and COVID-19 and the great possibility of biases of identification of smoking status in patients hospitalized with this infection, which can erroneously reflect as low prevalence of smokers in this group[30-32].

Toxicity aspects of tobacco smoke that make the smoker more vulnerable to the severity of covid-19 infection

The smoke generated by cigarettes and other tobacco products is an aerosol formed by more than 7 thousand chemical substances of different classes[33,34]. Among these components, it stands out the breathable particulate matter that functions as important inflammatory agent for lesions and thrombus in the lungs and blood vessels[35-39].

Regarding the nicotine, besides causing chemical dependence and acting as a promoting agent in carcinogenesis, stimulates the production of the peptide angiotensin II that leads to vasoconstriction, which causes important impact in the cardiovascular system, especially in the development of arterial hypertension[40-42].

However, hypoxia is one of the most significant elements in common between the COVID-19 physiopathology and smoking. Clinical observations in COVID-19 infected patients describe an intriguing condition of serious silent hypoxemia, of progressive character and little responsive to mechanical ventilation[16,43,44]. It is a fast evolution condition, that unchains an acute inflammatory process, with the increase of the level of fibrinogenesis and D-dimers, which tends to evolve with disseminated intravascular coagulation, thrombotic microvascular damages and a storm of inflammatory cytokines, resulting in higher vascular permeability, multiple failure of organs and death[45-49].

Among smokers, hypoxia is chronic and results from inhaling a considerable volume of carbon monoxide (CO) at each cigarette puff. The high binding affinity of CO for hemoglobin generates carboxyhemoglobin, damaging the oxygenation of tissues and organs and resulting in lower tolerance to physical activity and less aerobic capacity[50-56].

Potentialized by the effect of other toxic substances of tobacco smoke, among smokers, the hypoxia evolves with a physiopathological mechanism similar to the observed in COVID-19, however, with slower evolution characterized by blood vessels endothelium dysfunction and by chronic inflammatory process also mediated by cytokines[57]. This process, in its turn, contributes for a condition of hypercoagulability, characterized mainly by increase of platelets aggregation, increase of production of fibrinogenesis by the liver and dysfunctions in the process of fibrinolysis, important regulating mechanism of the hemostatic system that avoids the formation or removes the intravascular thrombus[58-62]. This chronic unbalance of coagulation and anticoagulation functions in smokers explains partially the increased risk of thromboembolic phenomenon. Under this perspective, it is plausible to consider that COVID-19 infected smokers tend to be more vulnerable to the severity of this condition for presenting chronic hypoxia secondary to smoking.

Biological aspects of smoking that make smokers more vulnerable to invasion of cells by the novel coronavirus

Studies that attempt to explain the relation between COVID-19 and smoking indicate that the increase of expression of ACE2 (angiotensin-converting enzyme 2) among smokers would be one of the main biological mechanisms responsible for greater risk of progression and complications of COVID-19 in this group. ACE2 is a protein found in the cellular membrane, where the virus binds to invade cells and inject its genetic material. Inside the cell, the virus starts to subvert the mechanism of cellular replication in favor of viral replication, process followed by destruction of the infected cells and expelling the virions (clones), that begin to invade adjacent cells that have ACE2 receptors. The successive process of invasions and replications will be more intense as higher is the quantity of these receptors in the organs previously to its infection[63-69].

In normal condition, ACE2 works as an important mediator of the renin-angiotensin endocrine system (RAS), present in the cells membranes, especially mucosa and organs as heart, kidneys, lungs and gastrointestinal tract[70]. RAS performs a relevant role in the regulation of the cardiovascular and neurovascular physiology[71,40]. In a simplified manner, RAS counts with two arms that function antagonistically to maintain the balance between vasoconstriction and vasodilation. In one

branch, acts the angiotensin converting enzyme (ACE), transforming angiotensin I into angiotensin II, has potent vasoconstrictor action and, when released in excess, contributes for the physiopathogeny of arterial hypertension. In the other arm, ACE2 acts, releasing angiotensin 1-7, that has vasodilation action important for proper myocardial and renal function. In short, these two enzymes (ACE and ACE2) act in a kind of seesaw in the two arms of RAS to keep the balance between vasoconstriction and vasodilation in the regulation of the neurovascular, renal and cardiovascular functions[70,72].

There are also evidences that the increase of expression of ACE2 represents the physiologic response to inflammatory processes in several tissues as of the lungs, liver, brain, in addition to developing a protective function in pathological conditions, as in atherosclerosis, cerebral ischemia, obesity, chronic renal disease and asthma. In these situations, the function of ACE2 would be to inhibit the cytokines, important inflammatory agents produced by the immune system, and its effects of proliferation, fibrosis and hypertrophy of tissues[73-75].

Among smokers, the increase of expression of ACE2 in pulmonary cells appears to be a dose-dependent protective response of the number of cigarettes smoked per day, because of the inflammatory processes unchained by the smoke of this product[68], mainly its small dimension breathable particulate matter of up to 2.5 micra (PM2.5) and CO[76-79]. It is plausible that these alterations also occur among users of electronic cigarettes or heat not burn cigarettes because of the presence of PM2.5 in the vapor they produce[80-82].

It is worth mentioning that the exposure to PM2.5, also present in the atmospheric pollution, was related to a higher rate of mortality by coronavirus in the USA and Italy[83-86].

Therefore, it can be presumed that, if the increase of ACE2 functions as an anti-inflammatory mechanism among smokers, on the other hand, while functioning as a receptor for the entry of the virus in the cell, ACE2 increases its vulnerability to a bigger viral load in the infection by COVID-19[87]. Still, it can be presumed yet that, during the evolution of the infection, the intensive destruction of the cells with receptors ACE2 by the virus reduces the anti-inflammatory protective effect of this enzyme and contributes for clinical condition[88]worsening. More recent studies have drawn attention to the storm of inflammatory cytokines that occur during the evolution of severer cases of COVID-19, a critical factor for multiple failure of organs and death[49,89,90].

Considering these aspects, it is possible that the presence of PM2.5 and CO in the secondhand smoke of tobacco products (the current that pollutes internal environments) can lead to the increase of expression of ACE2 in the lungs of passive smokers and also increase the vulnerability of this group to bigger viral load and odds of complications of infection by COVID-19[69,91-93].

Smoking can increase the risk of transmission of COVID-19?

Further to the risks of complications of COVID-19 among smokers, it was raised the hypothesis that the act of smoke by itself could increase the risk of transmission of this infection because it involves constant contact of the fingers with the lips, in case the hands had been in contact with any infected surface, including the cigarette itself. Similarly, the use of other products to smoke involving buccal sharing to inhale the smoke as waterpipes or *hookah*, could also facilitate the transmission of coronavirus among users and the community[94,95].

Studies showing that coronavirus disseminates through aerosol where it remains viable for until 3 hours[96-99] and the already understood relation between seasonal respiratory infections and levels of atmosphere pollution lead to the hypothesis that environmental pollutants can promote more permanence of the particles of the novel coronavirus in the air, causing its indirect diffusion, in addition to the known direct person-to-person[100-104] transmission. Under this perspective, it is plausible that the risk of transmission of the coronavirus applies also to passive smokers, that is, who breath the tobacco smoke in the environment. This smoke is an aerosol and includes, among other toxic substances, the PM2,5[91-93,105] mentioned before that can work as a vehicle for dissemination of the virus when persons smoke in contaminated collective ambient[106].

Psychosocial aspects of smoking and implications over COVID-19

In Brazil and in many other countries, the prevalence of smokers is concentrated in low income and low education groups[3,107,108]. Housing conditions of these groups, in their majority, do not permit a proper social distancing among family members, which can make them more propense to be affected by COVID-19[109-111].

It is still important to analyze the psychosocial effects of the pandemic over the national rates of smoking considering the context of economic and psychological instability, social isolation and difficulty of access to hospital care[112,113]. Studies about the impact of the pandemic showed more frequency of anxiety, stress and depression associated to fear of infection by the virus. Whereas smokers appear to use tobacco to cope with stress[114], it is essential to consider that this scenario of confinement, worry and uncertainties during the pandemic can reinforce still the dependence

of nicotine and stimulate smokers to smoke even more cigarettes in their houses, increasing the exposure of its relatives to tobacco smoke in the environment and its consequences, including those related to the transmission of COVID-19[64,115].

The benefits of reducing smoking while coping with COVID-19

Studies show that the level of expression of ACE2 in cells that make smokers more vulnerable to COVID-19 infection tends to stabilize among ex-smokers[68].

Furthermore, the cessation of smoking improves substantially other physiopathological aspects from smoking that can cause the complications of COVID-19. Hypoxia, resulting from CO chronic intoxication tends to disappear after the first 8 hours of continuous abstinence[53]. After one day without smoking, it is observed also the recovery of the endothelial dysfunction of the vessels and after two weeks of abstinence, the normalization of the platelets aggregation and the level of fibrinogen in the blood, which reduces the risk of thromboembolic and cardiac events among smokers[62,116].

These findings evidence the relevance of investing in measures to widen the cessation of smoking and prevent the initiation of smoking as strategies to reduce the impacts of COVID-19 among the population.

CONCLUSION

Equally COVID-19, smoking was also considered a pandemic by the World Health Organization (WHO) and the more cost-effective responses for coping with it were included in an international health treaty, the WHO Framework Convention for Tobacco Control (FCTC), in force for 15 years. Despite the evidences about the severity of smoking for public health, the national efforts for full fulfillment of this treaty are still delayed due to the big transnational tobacco corporations' interference.

Besides being a risk for several severe chronic diseases since 1990, smoking is classified as disease in the 10th Review of the WHO International Code of Diseases and considered a pediatric disease, because the majority of the smokers start smoking in the adolescence as a result of marketing strategies targeted to this group. However, despite the policies for its control, every day, thousands of young adults are still induced to try cigarettes and start smoking.

All the scientific evidences of the epidemiologic, biologic and psychosocial aspects or the negative impact of smoking in the transmission and complications by COVID-19 indicate that this risk factor will contribute to widen the morbimortality by the novel coronavirus and raise the expenses of the health system with equipment and supplies purchasing and organization of services.

Therefore, public policies to expand the access to the smoke cessation treatment and effective educational and legislative measures to reduce the young adults smoking initiation need to be prioritized urgently in the governmental strategic agenda of fighting COVID-19 and other future pandemics.

The vaccine against the COVID-19 pandemic is still in development. Nevertheless, the medication to stop the tobacco pandemic exists and depends on the prioritization of public health interest over the big tobacco corporations' economic lobby, safeguarding the wide WHO Framework-Convention of Tobacco Control implementation's.

CONTRIBUTIONS

Tânia Maria Cavalcante contributed substantially for the conception of the study, gathering, analysis and interpretation of data, wording and critical review. Cristina de Abreu Perez and Felipe Lacerda Mendes contributed in gathering, analysis and interpretation of data, wording and critical review. Alessandra Trindade Machado, Erica Cavalcanti Rangel, Renata Cristina Arthou Pereira, Rita de Cassia Martins and Angela Machado de Miranda Leal contributed with critical review. All the authors approved the final version published.

DECLARATION OF CONFLICT OF INTERESTS

There is no conflict of interests to declare.

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