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Cigarettes, Are They Harmful or Viricidal (Anti-COVID-19)? Why Some Smokers Are Severely Affected By SARS-Cov-2, Whilst Most Are Not Or Less Affected? A Controversial Minireview

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ABSTRACT

COVID-19 (Corona Virus Disease 2019) caused by novel Corona virus (nCov 2019) virus which was named later as Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) which is a global pandemic. As of 20 October 2020, more than 40 million people have been infected and more than 1.1 million deaths have been reported from COVID-19 worldwide. No evidence-based cure for infection and it is generally recommended to avoid transmission by social distancing, isolation and hygiene steps. In cultures around the world, cigarette smoking is rampant, and tobacco addiction leads to the deaths in more than 8 million people per year. Tobacco smokers are considered a low risk of serious COVID-19 infection due to unknown reasons. However, cross-infection and susceptible hygiene habits helped COVID-19 to cause deaths more than regular infection, as COVID-19 transmits by salivary droplets that lead to extreme lung pneumonia. Exhaled smoke, coughing or sneezing is created by smoking tobacco (cigarettes, e-cigarettes or waterpipe), aerosols usually containing SARS-CoV-2 in the air lead to contaminating different surfaces. Smoking is extremely controversial with regards to COVID-19 infection because most smokers are COVID-19 resistant, and others are susceptible

KEYWORDS: COVID-19; Tobacco smoking; cigarettes; ACE-2; nicotine

Introduction

COVID-19 is predominantly a respiratory tract disease characterized by acute respiratory clinical symptoms. Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) is the causative agent to this disease [1]. The virus discovered in Wuhan, Hubei Province, China, in December 2019 and grew into a pandemic that spread quickly worldwide [2,3]. Around mid-March 2020, a total of almost around 20K cases of COVID-19 were recorded, including 7876 cases deaths and most of those reported in China and Italy [4]. Viral transmission would happen as a result of close contact between infected and non-infected individuals. Entrance of SARS-CoV-2 virus to the body can occur via the mucosal tissues in the nose, mouth, upper respiratory tract, as well as the conjunctival mucosa[5]. Exposure to tobacco smoke results in inflammatory states in the lungs, such as increased mucosal inflammation and epithelial cell permeability, as

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well as expression of inflammatory cytokines, tumor necrosis factor alpha, overproduction of mucus, and decreased clearance of the mucosa[6-9]. In addition, cigarette smoke destroys the various protective systems of the respiratory system [10-12]. Common symptoms of COVID-19 include fever, diarrhea, sore throat, body aches, headache, cough, and shortness of breath[13]. Serious symptoms respiratory distress, renal failure, shock, and arrhythmia occur in about a quarter of symptomatic patients[14]. It is suspected that patients with established chronic disease (chronic lung disease, uncontrolled diabetes, coronary heart disease), immune-impaired state are highly and infected as a sever state[15]. Treatment for COVID19 patients requires symptomatic (antipyretics, analgesics) and supportive, with or without antiviral therapy[16].

Relationship between smoking and COVID-19:

The risk of serious infection is uncertain, but with COVID19 infections, older individuals (60 years and above) represents a higher mortality rate[17]. During cough, sneezing and conversation in close proximity, saliva as droplets forms can move from COVID-19 infected to healthy people[18-20]. Additionally, smoking tobacco (cigarette, e-cigarette and waterpipe) involves a frequently contact of saliva droplets with hands and involved surface of devices, which is a mainly source of viral infection spread[1,4,21,22]. Therefore, to prevent any transmission, World Health Organization (WHO) has published instructions and guidelines which must be followed so as to prevent as much as possible any route of viral transmission[23]. These include washing hands for at least 20 seconds by water and soap along with the promotion of disinfectants by using alcohol. To achieve social and healthy distancing meticulously by maintaining at least a 1-meter gap between people. No handshake is ultimately recommended, avoid contact with nose, mouth and eyes. It is also recommended to use elbows to cover face whilst coughing and sneezing then hand sterilization is highly recommended[23].

Smokers are a portion of the COVID-19 risk community. It can be inferred that the community increases the risk of infection to the point that smokers prefer to keep smoking items in their mouths without adequate prior hand hygiene, whether conventional cigarettes or electronic smoking devices (ESDs)[24-26]. Water-pipes, which are very prevalent in the younger populations (which is the causative agent of many cardiac disorders and malfunctions in the cardiovascular system) who mainly share the mouthpieces, promote the transport of COVID-19 disease[27-30]. World Health Organization (WHO) expressed concern about the possible prevalence of tobacco products from the use of COVID-19 disease[31]. With regards to water-pipe mouthpieces, the literature indicates that diseases such as oral herpes and tuberculosis are possibly transmitted[32,33]. The shared use of electronic smoking devices (ESDs) should be considered as contributing factor to SARS-CoV-2 transmission[34].

Nevertheless, efforts to stop smoking tobacco can not be over emphasized amid the COVID-19 pandemic. If the most important management techniques for containing this COVID-19 crisis are isolation and hygiene measures, quitting and restricting cigarette smoking may be one of the crucial measures to reduce viral spread. Strict smoking labels (Figure 1) must also be accepted by the general public and underlined by the authorities. Only in specified areas with strict hygiene measures (cigarette holders or filters) should smokers be put in isolation and smoking and good ventilation should be allowed. Smoking should be a solitary habit without people in the immediate vicinity being present. Smoking devices should be for single use and devices (conventional cigarettes, e-cigarette devices, water-pipes) should not be reused, exchanged or

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shared. After single use, all cigarette stubs and devices and their attachments should be disposed of as contaminated[35].

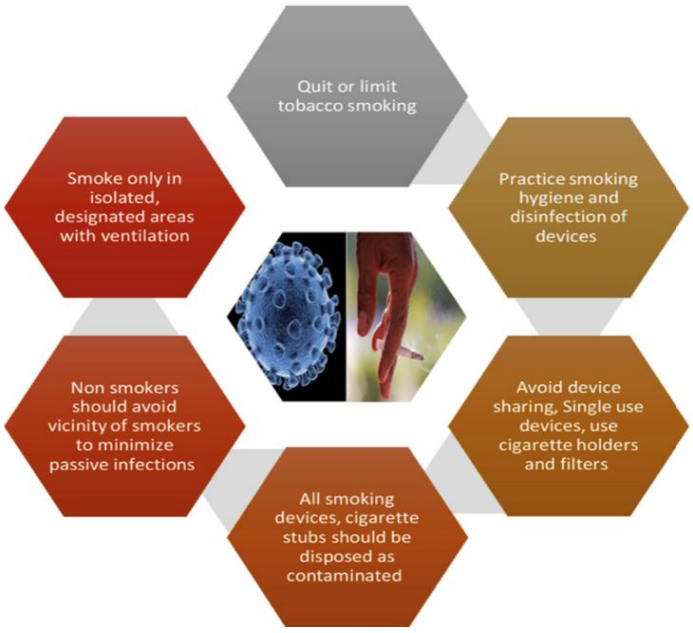

Figure 1. COVID-19 Transmission and Tobacco Smoking Etiquettes

Effect of smoking on immune response against SARS-CoV-2:

Cigarette smoke has been shown to up-regulate inflammation and to down-regulate effective immune function by stimulating the nuclear factor kappa-light-chain-enhancer of activated B cells, tumor necrosis factor-a (TNFα), interleukin-1 beta (IL-1β) and neutrophils[36]. This effect is proportional to a rise in smoking and does not subside immediately after cessation of use [37-39].SARS-CoV-2 patients have been shown to have elevated levels of tumor necrosis factor inflammatory cytokines-alpha, IL-2R, and IL-6 on presentation, and the virus causes lymphocytopenia[40,41]. Animal and human cell studies suggest that nicotine increases the incidence of infectious diseases such as influenza and increases viral replication in cells with a central role in innate mucosal immunity by suppressing antiviral functions and altering cytokine patterns[34].

Available information from China indicates a lower number of hospital admissions among the smoking population than expected. Crude (non-age-stratified) smoking prevalence in China is estimated to be 54% among males and 2.6% among females[42]. However, a study of 8 Chinese studies with smoking status data indicates fewer hospitalized smokers than national prevalence estimates would suggest[43]. For 1085 patients hospitalized with COVID-19, smoking status was recorded in the largest of these studies [13], 12.6% were current smokers, 1.9% were former smokers and 85.4% were never smokers. At 12 percent, 24 percent and 4.8 percent, present and former smokers had poorer results than ever smokers[13].

Smoking is physiologically harmful related to angiotensin-converting enzyme-2 (ACE-2) and to the possible consequences of respiratory viruses[44]. In addition, Middle East Respiratory

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Syndrome Coronavirus (MERS-CoV) that triggered a minor coronavirus outbreak in 2012-2015 had the less clinical features as the current COVID-19 disease[45]. A correlation between smoking status and fatality rate was also suggested by reports. In addition, SARS-CoV-2 interacts at the alveolar level with the Angiotensin-Converting Enzyme 2 (ACE 2) receptor to enter the cell and induce the disease[46]. By agitating the immune response with increased development of pro-inflammatory cytokines, in particular IL-10, IL-8 and IL-1β [47,48]the increased ACE-2 expression mediated by COVID-19 entry will lead to respiratory dysfunction. With ACE2 being highly expressed among smokers as well as healthy people in the lungs[49].

A study showing that smoking is associated with increased ACE 2 receptor expression and may give smokers a higher susceptibility to COVID-19 has been reported by Wang et al. [14,50]ACE2 gene expression has recently been documented to be higher in ever-smokers relative to never-smokers in normal lung tissue in a study of lung adenocarcinoma patients, after age, sex, and ethnicity analysis. Several studies show that gene expression and subsequent levels of receptors are high in current smokers' oral epithelium[50-52].

Human studies have shown that smoking cigarettes controls the expression of ACE2 in the lungs, which could lead to an increased risk of infection with SARS-CoV-2. Patients with coronavirus exhibit elevated levels of C reactive protein (CRP) and D-dimer[50,51]. In smokers, these diagnostic indicators of thrombosis are often updated[52,53]. One study appears disseminated intravascular coagulation in 71% of lethal cases of COVID-19 compared to 0.4% in survivors 46. High levels of D-dimer (> 1μg/ L) in hospital admissions raise the risk of death by 18 times[54-56]. The mechanism of these complications is still unclear, but the importance of the effect of smoking on the endothelium and COVID-19 is suggested.

Controversial aspect: Tobacco works well as COVID-19 blocker/inhibitor (Smokers are COVID-19 resistant!)

One of the most surprising finding with regards to SARS-CoV-2 blocker/inhibitor is tobacco according to[57] who found that smokers might be protected from COVID-19 due to the nicotinic effect of tobacco which consists of nicotine and tan that targets acetylcholine receptors. Moreover, [58]applied a cross-sectional study performed on in- and out-patients both gender who were hospitalized for COVID-19 positive and the results showed that smokers developed mild to moderate symptoms by comparison with non-smokers who suffered from severe symptoms. Above studies are not the only research done to highlight the negative effect of smoking on COVID-19 cases, further studies reported that there is no or very little (negligible) impact of smoking on respiratory viral infections[13,17,54,59,60] which supports the idea that suggest smoking has no impact on COVID-19 patients. Finally, it has been claimed that smoking is not related to the level of severity of COVID-19 patients [61-67].

Conclusions

Smoking and vaping raise the risk of becoming contaminated, hence infected and that is why the population should remember with SARS-Cov-2 during the pandemic of COVID-19 .Smokers should realize that not only are they more likely to produce COVID-19, but also to have a COVID-19 inadequate prognosis .Emphasizing the importance of avoiding smoking and encouraging the use of the tools available To assist smokers in this decision, especially in those

techniques that do not require presence in health care centers, such as quit lines, applications, video consultations, teleconsultations. Discouraging the use of hookahs, using electronic delivery systems for nicotine (electronic cigarettes or vapers) and heated tobacco products since, aside from spreading the virus, they can serve as fomites. Emphasizing the value of ensuring a 100 percent smoke-free public and private atmosphere during quarantine. On the other hands, tobacco can play an anti-COVID-19 substance through its constituents (nicotine and tan) which are thought to possess anti SARS-CoV-2 effect. Therefore, it is controversial for decision-makers to take an action whether to keep smoking/ stop it soon based on general health condition and the way tobacco works.

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