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Cigarette Smoking: A Major Cause of Emphysema

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Abstract

Cigarette smoking or tobacco smoking is still a huge problem in the present day. Not only does smoking affect smokers' health but it also affects the people surrounding them as well. Cigarette smoking is the main cause of emphysema and other chronic obstructive pulmonary disease worldwide. Tar and other irritants in tobacco smoke can affect the balance of protease-antiprotease which can trigger the destruction of the alveoli thus causing emphysema. The symptoms of emphysema include shortness of breath, wheezing, heavy breathing, tightness in the chest, and frequent coughing. Although emphysema sounds scary, emphysema is a disease which very rarely occurs on its own but is usually caused by environmental influences and there are precautions that we can take to avoid it. Examples of these precautions are avoiding smoking, avoiding other respiratory irritants, or even wearing masks in areas with air pollution. These precautions will help reduce the risk of emphysema and reduce the chronic obstructive pulmonary diseases related deaths in populations around the world.

Keywords: Smoking; emphysema; protease-antiprotease; chronic obstructive pulmonary disease(COPD).

1. Introduction

Cigarette smoking became a social norm in the first half of the 20th century. In the 1950s, 50% of the population of industrialised countries smoked [1]. Smoking was seen as acceptable behaviour in all areas, whether it was work, bar or home. Although in recent years where smoking is strongly discouraged and regulations are implemented to make it harder to sustain smoking, cigarette smoking is still a huge problem and is the leading cause of preventable diseases worldwide [2]. A typical cigarette is made from tobacco, wrapping paper, filter, and other additives. Burning cigarette smoke releases thousands of chemicals, including at least 70 known to cause cancer. These chemicals are called carcinogens. Chemicals in cigarette smoke include nicotine, hydrogen cyanide, lead, and carbon monoxide [3]. Long-term exposure to tobacco smoke can lead to an increased risk of emphysema. In fact, the leading cause of emphysema is tobacco smoking [4]. Common symptoms of emphysema include shortness of breath, frequent coughing, and chest tightness [5]. This literature review aims to explore and discuss the major effects of tobacco cigarette smoking, especially in the aspect of the lungs. And to encourage people to stop smoking cigarettes and also discourage people to start smoking.

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2. Nicotine Addiction

Nicotine ($C_{10}H_{14}N_2$), can be considered the major cause of cigarette addiction. Consuming any tobacco-related product can cause nicotine addiction, this is because nicotine is an addictive central nervous system (CNS) stimulant [6]. As nicotine in smoke particles is inhaled, nicotine moves from the lungs to the brain where it binds to nicotinic cholinergic receptors (which normally bind with acetylcholine). The binding of nicotine allows the entry of sodium and calcium cations into the cells which leads to the activation of voltage-dependent calcium channels where more calcium is allowed to enter, releasing neurotransmitters. Dopamine is one of the neurotransmitters released. Dopamine signals are sent when you experience something pleasurable and are important for the reinforcing effects of self-administration on nicotine, other drugs of abuse and urge such as eating. Additionally, nicotine stimulates the release of GABA, which inhibits dopamine production, as well as glutamate, which enhances dopamine release [7].Some nicotinic cholinergic receptors become desensitized to nicotine with time, whereas others do not. As a result, GABA-mediated inhibitory tone is diminished but glutamate-mediated excitation is maintained, boosting the excitation of dopaminergic neurons and improving responsiveness to nicotine [8].

3. Carbon Monoxide

The product of incomplete combustion is carbon monoxide and water. Incomplete combustion happens when there is not enough oxygen in the air or the concentration of oxygen is too low. The gas produced is colourless and odourless. There are various sources of carbon monoxide and all of them are combustion sources. These combustion sources include vehicles, power plants, waste incinerators, domestic gas boilers, and cigarettes all emit carbon monoxide to an extent.

Carbon monoxide has a 210 times higher affinity for haemoglobin than oxygen [9]. Therefore, even low concentrations in the environment can cause toxic levels of carboxyhemoglobin. This reduces the amount of oxyhemoglobin formed and reduces oxygen release. Moreover, the affinity of carbon monoxide for myoglobin is even greater than that for haemoglobin which myoglobin is an oxygen-binding protein that supplies oxygen to muscles. Long and saturated exposure to carbon monoxide can lead to severe cases of carbon monoxide poisoning [10]. If carbon monoxide has been bound to cardiac myoglobin it can potentially cause myocardial depression, hypotension and arrhythmias [11]. With extreme poisoning of carbon monoxide, coma, convulsions, and cardiopulmonary arrest may occur. Constant exposure to carbon monoxide can happen between smokers and non-smokers. Second-hand smoke can cause both adults and children premature death. In the United States, second-hand smoke death is estimated to cause about 34,000 people deaths each year from heart disease [12]. It increases the risk of heart disease by an estimated 25-30%.

4. Tar

Tar is a natural substance distilled from coal, wood, petroleum or peat, forming a dark flammable viscous liquid. In terms of smoking, tar's composition consists of more than 4,000 chemicals that can cause short-term and long-term effects on health [13]. Its thickness and viscosity are among the tar's physical characteristics. The

majority of substances that reside in tar are mutagenic and carcinogenic agents that damage the smoker's lungs. It is one of the most contributors to the flavour and scent of cigarette smoke that have an impact on smokers' behaviour. Tar, along with nicotine, has also traditionally been quantified in tobacco smoke for an exceptionally significant period of time. It is widely regarded as the most dangerous component of tobacco smoke.

The tar that resides in tobacco smoke, can accumulate a sticky film inside your lungs as you inhale the smoke [14] . Thus, can cause detrimental effects on the lungs and ultimately lead to lung cancer, emphysema, or COPD when the lungs become more and more tar-filled from smoking. This cause a change in colour from healthy lung tissue turning into greyish black, the more tar builds up within the lungs. The principal consequence of the tar is that it paralyzes and can eventually kill cilia in the airways [15]. Cilia are tiny hair-like organelles that line up and are attached to the trachea. They aid the removal of debris out of the airways and secrete mucus to prevent respiratory infection from the lungs [16] . The compounds in tar, however, can more seriously contaminate the lungs if they are damaged. Some of these toxins are released when you exhale or cough, while others settle and remain in your lungs. This can eventually result in lung illness and disorders including emphysema, bronchitis, and lung cancer. Depending on how cigarettes and other smoked tobacco products are created, they may contain varying degrees of tar. Additionally, the effects of tar can discolour and make teeth as it seeps into the enamel of the tooth and also makes fingers yellow.

5. Chronic obstructive pulmonary disease (COPD)

It is one set of disorders that induce breathing difficulties and airflow obstruction. Over time, they progressively deteriorate. According to the Centers for Disease Control and Prevention (CDC), about 15.7 million Americans have COPD [17]. Furthermore, women are more likely to have COPD than men, though it's crucial to remember that women who smoke have a 50% higher chance of developing the disease than men. Females with severe COPD are also more likely to be hospitalized and succumb to respiratory failure. Furthermore, individuals with a history of asthma, those 65 and older, and current or previous smokers are often more susceptible to developing COPD [18].

Stretchy airways and air sacs are signs of healthy lungs. Due to their elasticity, this enables the air sacs to inflate and deflate freely when the individual inhales or exhales. People with COPD have less air flowing into and out of their airways, which is often caused by the airways and sacs becoming overly compliant, especially in emphysema, and losing their elastic rebound, resulting in alveolar deterioration [19]. The thickening and inflammation of the airway walls resemble chronic bronchitis. Asthmatic patients' airways produce more mucus, which inhibits airflow [20].

COPD is classified into two major types: emphysema and bronchitis. However, some individuals can have both varieties of COPD [21]. Emphysema is when the alveoli, or the walls of the air sacs, are damaged and lose their shape and capacity to retract during the exhalation or also known as the expiratory phase of the breathing cycle. This then results in trapped air in the lungs. An airway obstruction cycle is brought on by this trapped air, which keeps the alveoli from contracting. These changes cause the lungs to expand excessively, which decreases gas exchange. This reduces a person's capacity to remove carbon dioxide from circulation and makes it more

difficult for them to breathe and oxygenate their blood efficiently. In cases of chronic bronchitis, the lining of the airways remains red and swollen. As a result, there is swelling and a substantial amount of mucus production. These side effects make it difficult for people to breathe [22].

6. Stages of COPD

The four phases of COPD can be categorized as follows: mild COPD, moderate COPD, severe COPD, and very severe COPD. Mild COPD is classified as Stage 1. Some people may also have a continuous cough in addition to having mild breathing restrictions. They may cough up sputum, a mucus-saliva mixture. The aberrant lung function that they are experiencing at this point might not be known to them. Moderate COPD is classified as stage 2. In Stage 2, the airflow restriction becomes more severe, and persons frequently feel exercise-related breathlessness. Usually, at this point, patients begin looking for medical assistance. Severe COPD is classified as stage 3. In stage 3, a person's airway is further restricted, resulting in increased shortness of breath. This is accompanied by a decline in exercise tolerance. The frequent episodes of deteriorating symptoms impair one's quality of life. COPD in stage 4 is classified as severe. In stage 4, people experience severe airflow restrictions and a significantly diminished quality of life, while episodes of worsening symptoms may become lethal [23].

7. Types of Emphysema

There are various types of emphysema with each type being categorised by certain features unique to the type of emphysema. These types of emphysema are panacinar emphysema, Distal acinar or paraseptal emphysema, and Centriacinar emphysema [24].

Distal acinar or paraseptal emphysema

Expanded airspace near the acini's perimeter is a characteristic of distal acinar or also known as paraseptal emphysema. The lesion often has a small area, mostly affects the dorsal aspect of the upper lung, is frequently fibrotic, and may coexist with other forms of emphysema. Although the patient normally has no symptoms, the disease is thought to be a factor in young adults developing pneumothorax [25].

Panacinar emphysema (permanent destruction of the airspaces (alveoli) distal to the respiratory bronchioles)

The air passage connecting the respiratory bronchioles to the alveoli is uniformly dilated in panacinar emphysema, which causes emphysematous alterations to be dispersed evenly within secondary lobules [26]. In a gross specimen of a normal lung, the respiratory bronchioles and alveolar ducts have somewhat larger lumens than the nearby normal alveoli. With the widening of the alveolar gap in very early panacinar emphysema, this difference tends to diminish and look "monotonous." Alpha 1-antitrypsin deficiency is believed to play a substantial role in the development of panacinar emphysema, despite its extremely low occurrence [27]. The majority of cases found in surgical or postmortem specimens are unconnected to these disorders, despite reports of alternative etiologies including Swyer-James syndrome and ritalin addiction. Centriacinar emphysema and panacinar emphysema differ in the following ways: In contrast to centriacinar emphysema, bullous growth is less common and the airway has a tendency to become smaller. The lower lung field is where the disease is most

prevalent, whereas the upper lung is where centriacinar emphysema is most prevalent [28].

Centriacinar emphysema (long-term, progressive lung disease)

The most prevalent form of pulmonary emphysema, known as centriacinar emphysema, is characterized by an expansion of the centriacinar airspace, with the effect primarily occurring in the proximal respiratory bronchioles and normal distal alveolar ducts and sacs [29]. The disease mostly affects the second and third respiratory bronchioles, and the degree of lung parenchyma loss varies from lobule to lobule in most cases. The majority of emphysema seen in heavy smokers is centriacinar emphysema, which is thought to be intimately associated with dust inhalation and cigarette smoking. The upper lobe or the superior segment of the lower lobe is typically affected by the condition [30]. The exact causes of this distribution are unknown, however, they could include regional variations in perfusion, leukocyte transit time, removal of accumulated dust, and pleural pressure. Because of zonal disparities in lymph flow and respiratory kinetics, the inner zone is more severely impacted than the outer zone [31].

One of the three primary pulmonary emphysemas caused by long-term, heavy smoking is centrilobular emphysema, also known as centriacinar emphysema. 85% to 90% of all COPD cases in patients who are heavy smokers have been diagnosed or have progressed to centrilobular emphysema. Its symptoms include weariness, chest tightness, and shortness of breath (dyspnea). It affects the central respiratory bronchioles, which are primarily located in the upper lobe region and apices inside the upper and lower lobes of the lung. As the condition worsens, these symptoms may become more severe. Centrilobular emphysema lung function efficiency declines from around 80% in the early stages to below 30% in the late stages [32].

Effects on the surface area to volume ratio of the lungs

To enhance gas exchange within the lungs, the surface area to volume ratio of the lungs must be high. However, over time the alveoli become harmed as a result of emphysema. Instead of having many little air spaces, the inner walls of the air sacs deteriorate and rupture, resulting in bigger air spaces [33]. This causes the surface area to volume ratio of the lungs to drop, which results in less effective gas exchange and lower blood oxygen levels. Additionally, because the injured alveoli are unable to function properly during exhalation, old air is stuck and cannot be exchanged for new, oxygen-rich air [34].

Pathogenesis of Emphysema

Studies on both humans and animals provide credence to the idea that the imbalance of protease-antiproteases may be a key factor in the pathophysiology of COPD [35]. In COPD, excessive neutrophil activation and accumulation upset the protease-antiprotease balance and start the process of lung damage. The endogenous secretory neutrophil elastase inhibitors, which are prevalent in the respiratory tract and regulate neutrophil elastase activity, counteract the proteolytic action of neutrophil elastase. The protease inhibitor -1-antitrypsin is crucial for regulating protease activity. The proteolytic activities of neutrophil elastase, proteinase-3, cathepsin G, and neutrophil serine protease-4 are all potently controlled by this inhibitor. Emphysema is caused by a lack of -1-antitrypsin and can be successfully treated by exogenous -1-antitrypsin supplementation. According to

studies, treating -1-antitrypsin deficiency in COPD patients lowers mortality and slows emphysema progression. Members of the chelonianin family of molecules, such as secretory leukocyte protease inhibitor (SLPI) and elafin, can also inhibit neutrophil elastase (NE) and regulate proteolytic activity. Since respiratory tract epithelial cells largely produce SLPI and elafin, it appears that they may be crucial in the development of COPD.

Because of genetic abnormalities, insufficient production of -1-antitrypsin, or inactivation of -1-antitrypsin by oxidants brought on by smoking, the equilibrium of protease-antiprotease may be disturbed. The pathophysiology of COPD has also been connected to genetic differences (deficiencies of -1-antitrypsin). Neutrophil elastase is overexpressed and non-regulated in the absence of -1-antitrypsin, which leads to lung parenchymal damage [36]. The connection of elevated leukocyte elastase concentration supports the crucial role of neutrophil elastase in anti-trypsin-deficient COPD [37]. A protease-anti-protease imbalance in the lung can also be brought on by smoking and environmental pollutants, which decrease the functional activity of -1-antitrypsin in the lung interstitium and increase the amount of elastolytic proteases released in the lung's "alveolar" lining fluid. According to the research, oxidative stress also makes anti-proteases like SLPI and -1-antitrypsin less effective [38], which speeds up the decomposition of elastin in the lung parenchyma. Investigating the function of proteases and their control is important since the expression of proteases and their inhibitors contributes significantly to the pathophysiology of COPD [39].

Treatment

Although various therapies can aid with symptom relief and delay the course of the disease, emphysema and COPD cannot be cured. To treat the symptoms, doctors can prescribe certain drugs. Examples of these medications include bronchodilators, inhaled steroids, and antibiotics. By relaxing restricted airways, bronchodilators can aid with coughing, shortness of breath, and breathing issues. Aerosol sprays containing inhaled steroids, such as corticosteroids, can be used to ease shortness of breath and reduce inflammation [40]. In terms of antibiotics, they are appropriate if you have a bacterial infection such as acute bronchitis or pneumonia.

Additionally, there are treatments available for emphysema and COPD patients. A pulmonary rehabilitation program is a typical form of treatment that patients receive. A pulmonary rehabilitation program can teach you breathing strategies and exercises that could help you feel less out of breath when exercising and enhance your performance. Additionally, if the patient has a severe case of emphysema and a low blood oxygen level as a result, they can use oxygen frequently at home and while activity may offer some relief. Numerous people consume oxygen constantly. Usually, it's given to you through a little tube that fits in your nostrils [41].

The severity of emphysema will determine whether doctors may recommend one form of surgery or the other. A treatment called lung volume reduction surgery involves the removal of tiny wedges of diseased lung tissue. The remaining lung tissue expands and functions more effectively after the unhealthy tissue is removed, which improves breathing. If other treatments have failed and the lung is badly damaged, a lung transplant may be an option.

Alternative to tobacco smoking

It can be quite hard for a chronic smoker to quit smoking suddenly, so there are alternatives to tobacco smoking to help smokers to stop smoking. Popular alternatives include nicotine patches, nicotine chewing gum, lozenges, tablets, mouth sprays and inhalers [42]. These products can help suppress the urge to smoke because they deliver nicotine and help raise the nicotine levels in your body. However, the most effective product as an alternative to smoking tobacco is e-cigarettes. But e-cigarettes or vaping have shown to increase the risk of emphysema and thus should only be used as a last resort if other nicotine replacement products fail [43].

8. Findings and discussions

Cigarette smoking is by far the biggest cause of emphysema and other COPDs. Cigarettes contain various substances including tar, carbon monoxide, nicotine which are health-damaging and also addictive. The most lung-damaging substance in cigarettes is tar, it contains substances which irritate the lungs and thus can cause emphysema. The majority of emphysema seen in heavy smokers is centriacinar emphysema. Furthermore, the mechanisms which cause emphysema include protease-antiprotease imbalance and oxidative stress. There are numerous serious symptoms regarding emphysema which the victim of the disease can suffer from like coughing, shortness of breath, and exhaustion. These symptoms can become severe enough to cause serious complications and lead to death.

9. Conclusion

Due to the biases we have against cigarette smoking, the findings are argueably one sided in regards to only viewing cigarette smoking in a negative manner and therefore the findings are dominated by facts and disussions against cigarette smoking. However, the biases are justified as it is proven that cigarette smoking is undoubtly linked to the development of emphysema and other COPDs. Cigarette smoking should not be a social norm as it can cause serious consequences in smokers themselves and also to the people around them. It is crucial to not start smoking to prevent emphysema. If the individual struggles to stop smoking, he/she should seek help and maybe even try nicotine replacement products to assist in permanent abstinence from smoking.

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