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Review

Community-Acquired Pneumonia Among Smokers☆

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ABSTRACT

Recent studies have left absolutely no doubt that tobacco increases susceptibility to bacterial lung infection, even in passive smokers. This relationship also shows a dose-response effect, since the risk reduces spectacularly 10 years after giving up smoking, returning to the level of non-smokers.

Streptococcus pneumoniae is the causative microorganism responsible for community-acquired pneumonia (CAP) most frequently associated with smoking, particularly in invasive pneumococcal disease and septic shock.

It is not clear how it acts on the progress of pneumonia, but there is evidence to suggest that the prognosis for pneumococcal pneumonia is worse.

In CAP caused by *Legionella pneumophila*, it has also been observed that smoking is the most important risk factor, with the risk rising 121% for each pack of cigarettes smoked a day.

Tobacco use may also favor diseases that are also known risk factors for CAP, such as periodontal disease and upper respiratory viral infections.

By way of prevention, while giving up smoking should always be proposed, the use of the pneumococcal vaccine is also recommended, regardless of the presence of other comorbidities.

Neumonía adquirida en la comunidad en fumadores

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RESUMEN

En estudios recientes ha quedando quedado perfectamente establecido que el tabaco incrementa la susceptibilidad a la infección bacteriana pulmonar, incluso en fumadores pasivos. Este efecto muestra también dosis-respuesta, ya que disminuye espectacularmente el riesgo 10 años después de abandonar el hábito tabáquico, situándose a niveles de no fumadores.

Streptococcus pneumoniae es el microorganismo causante de neumonía adquirida en la comunidad (NAC) que más se ha relacionado con el tabaquismo, especialmente en situaciones de enfermedad neumocócica invasiva y shock séptico.

Su influencia sobre la evolución de la neumonía no parece clara, aunque existen evidencias que sugieren un peor pronóstico de la neumonía neumocócica.

En NAC causadas por *Legionella pneumophila* también se ha observado que el hábito tabáquico es el factor de riesgo más remarcable, ya que puede suponer un aumento del riesgo del 121% por cada paquete diario de cigarrillos consumidos.

Por otro lado, el consumo de tabaco puede también favorecer la presencia de enfermedades que a su vez son factores de riesgo conocidos de NAC, como enfermedades periodontales e infecciones víricas de la vía aérea superior.

Como medida preventiva, si bien cabe proponer el abandono del tabaco, también es recomendable la vacuna neumocócica, independientemente de la presencia de comorbilidad.

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The adverse effects of tobacco smoking make it one of the most important risk factors for major chronic cardiovascular and respiratory diseases. In some of these, tobacco use may worsen prognosis, while for others there is a clear causal relationship.

Chronic obstructive pulmonary disease (COPD) and lung cancer are among the most common smoking-related diseases, but there is also evidence linking smoking with diseases such as asthma, interstitial and allergic diseases, and pulmonary infections.[1] Indeed, the airway is constantly exposed to microorganisms, but the healthy lung has sufficient defense mechanisms to prevent microbial invasion (effective mucociliary clearance, epithelial barrier integrity, alveolar macrophages that recognize and phagocytize invading microorganisms). Any failure of these mechanisms may result in microorganisms spreading to the bronchial tree, triggering community-acquired pneumonia (CAP), which remains a major cause of morbidity and mortality in developed countries. In the general adult population, the annual incidence of CAP varies between 1.6 and 13.4 cases per 1000 inhabitants, with a hospitalization rate of between 22 and 51% and a mortality rate of 3%–24%[2–4] that has not changed in recent years, despite the preventive measures undertaken.[5]

Smoking and Pneumonia

The most important risk factor for CAP is age. So much so, that the incidence triples or quadruples when age is >65 years.[2] The reason is unclear, but several factors may be involved, related to immune senescence due to weakness (innate and adaptive) of the immune system, increased asymptomatic aspirations in this age group,[6] or the convergence of other risk factors (RF) that do not acquire statistical significance in younger people, but that take center stage in older age groups, possibly due to an additive effect. One of these factors may be tobacco smoking, the main RF for COPD, which in turn is one of the main RFs for CAP. Thus, it is often difficult to determine the specific weight of smoking in the development of CAP, especially considering that smoking is associated with lower socioeconomic status, poor diet, increased alcohol consumption, and reduced physical activity, that are also RFs for respiratory infection.[7] Nevertheless, enough studies using statistical analysis with logistic regression models are now available to allow the differentiation of any confounding factors, showing that tobacco smoking in itself increases the risk of pneumonia. In this regard, a population-based study[2,3] was published that demonstrated an increased risk of CAP in smokers that was also directly related to the duration of tobacco consumption and the number of cigarettes consumed. Concurrently, it has been shown that this risk disappears when smokers quit. In fact, after 5 years, the risk decreases by 50%.[3] Moreover, if we consider that one of the criteria for causality between two factors is dose-response, the increase in risk associated with an increase in intensity of consumption and the overall amount of tobacco consumed further reinforces the notion that tobacco smoking is a direct causal agent of CAP. On the other hand, we know that tobacco smoking causes morphological changes in the epithelium of the bronchial mucosa, with loss of cilia, mucous gland hypertrophy and increased goblet cells that may favor the presence and spread of microbes in the bronchial tree. An inflammatory reaction is produced in the airway causing macrophage and neutrophil activation that releases proteases. Oxidative stress and cytokine release are triggered, leading to both innate and adaptive immune response.[8–14] This may in turn make the bronchial mucosa epithelium more sensitive to the inflammatory aggression of the infection itself.[15–17] Moreover, it is now known that tobacco smoking inhibits some of the key functions of the innate and adaptive response, including the response of two Toll-like receptors (TLR2),[18] nuclear factor kappaB (NF-κB),[8] CD4-lymphocyte proliferation (LTCD4),[12,19] maturation of dendritic cells,[10] and opsonization and phagocytosis capacities.[20] Thus, tobacco smoking can alter immunity against infection, affecting the modulation of intra- and intercellular signaling of epithelium and immune cells, and suppressing the activation of important elements of the innate and adaptive immune response.[17,21] The fact that tobacco smoking increases susceptibility to bacterial infection is well established.[22,23]

Passive Smoking and Pneumonia

Passive smoking is considered a major epidemiological problem. In 2004, an international study including 192 countries found that 40% of children, 33% of male non-smokers and 35% of female non-smokers, were passive smokers.[24] There were wide geographical variations that could be explained by the different stages of the tobacco smoking epidemic in the country surveyed, because passive smoking is directly related to active smoking rates. In the year 2005, prevalence data in Spain estimated that about 50% of adults were exposed to second-hand smoke.[25] Later, as in most developed countries, legislation was introduced to regulate tobacco smoking in public places. This has reduced exposure to tobacco smoke by approximately 20%–25%, due to falling consumption in public places and in the workplace, but not at home. Accordingly, in recent years there has been growing interest in understanding the effect of passive tobacco smoking and some studies suggest that it could also involve a higher risk of respiratory infections in both the children of smoking parents,[26,27] and in adults.[28,29] Allowing smoking in the home has also been shown to be an important predictor of health loss in elderly people with CAP.[30] In fact, lesions in the respiratory epithelium, connective tissue and vascular endothelium of the lung caused by tobacco smoke can occur even at low smoke concentrations,[31] supporting the notion that exposure to tobacco smoke could be an important risk factor for CAP development in passive smokers.

Two separate case-controlled,[32] population-based studies have also demonstrated that passive smoking is a risk factor for developing pneumococcal bacteremia in immunocompetent adults, resulting in an odds ratio (OR) of 2.6 and attributable risk (AR) of 31% in subjects aged <65 years,[28,33] and OR 2.2 and AR 13% in those over 65 years of age.[28,32]

Smoking and Pneumococcal Pneumonia

The most common causative organism of CAP, regardless of care level and severity, is *Streptococcus pneumoniae*. This has also been shown to be the agent most frequently linked to smoking, especially in patients with COPD. An *in vitro* study has shown increased adherence of *S. pneumoniae* to the epithelial cells in the oral cavity of smokers,[34] persisting for up to three years after smoking cessation. This may produce greater oropharyngeal colonization and lead to greater chance of developing CAP.

Smoking has also been related with invasive pneumococcal disease (IPD), which in approximately 80% of cases is due to pneumonia.[35] This association was reported in a study by Pastor et al. in 1995, with an OR of 2.6 in smokers between 24 and 64 years of age and OR of 2.2 in smokers older than 65 years. Attributable risk (AR) was 31% in the first group and 13% in the second group.[3] Another population-based, case-controlled study[28] also highlighted that smoking is the largest independent RF for IPD in immunocompetent adults, with an OR=4.1 in current smokers (AR 51%). Furthermore, there is a dose-response effect, and smoking cessation dramatically reduces the risk after 10 years, when it becomes the same as that of nonsmokers.