



Tuberculosis and tobacco smoking.

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Abstract

Tuberculosis and tobacco smoking are two major public health problems which are causing a heavy mortality worldwide. Tobacco smoke increases the risks of *Mycobacterium tuberculosis* infection, of severe TB and death from TB. In emerging countries, quitting smoking is a means of controlling the TB epidemic. Smokers with TB are less compliant with TB medications, justifying smoking cessation support. Helping to quit smoking increases adherence to treatment of tuberculosis and tobacco abstinence rates among patients treated. It requires the involvement of every health-care professional.

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Introduction

Tuberculosis and tobacco smoking are two major public health problems worldwide causing million deaths every year. The major drivers of the tuberculosis epidemic are in the last two decades, the spread of HIV and the emergence of drug resistant tuberculosis but other risk factors are involved among which tobacco smoking; it is estimated that 13% to 20% of tuberculosis cases worldwide can be attributed to tobacco smoking [1]. Active and passive smoking are independent risk factors for TB infection, progression to pulmonary TB, severe disease and mortality [2]. Smokers suffering from TB are less compliant with TB treatments [3]. However, smoking cessation can improve the course of the disease, the observance of the treat-

ment and have an impact on the incidence of the disease. The World Health Organization has recommended a co-ordination between national TB and tobacco control programs [4]. The involvement of healthcare professionals in helping smokers with TB to quit smoking is required.

Influence of tobacco smoking on tuberculosis

Tuberculosis and tobacco smoking prevalences

In 2014, tuberculosis has been the cause of 9.6 million incident-cases and 1.5 million deaths worldwide [5]; at the same time tobacco smoking was causing 6 million deaths [6]. Smok-



ing has risen in emerging countries, in which 80% of tobacco is consumed [3]. In these countries more people with TB smoke now than ever [7]. Compared with people without TB, prevalence of smoking is higher in people suffering from TB [7].

Effects of Tobacco smoking on TB course.

Smokers have an increased risk of infection if exposed to *Mycobacterium tuberculosis* [8] and have an elevated risk of active TB if infected [9]. For tuberculous infection, the cross-sectional study of Singh, et al [10]. conducted in India found a OR of 2.68 (95% CI:1.52-4.71) with passive smoking; the meta-analysis of Slama, et al [11] found a pooled OR of 1.8 (95% CI:1.5-2.1) with active smoking. This study [11] highlighted a pooled OR of 2.6 (95% CI: 2.1-3.4) for the association of active smoking and pulmonary TB and of 3.4 (95% CI:2.0-5.5) with passive smoking. Tobacco smoking increases the risk of dying of TB and causes a significant risk of tuberculosis recurrence despite treatment [12]. All the risks linking tobacco and tuberculosis are dose dependent on smoking (duration and daily consumption) [2]. A study based on a mathematical modelling has estimated that smoking could raise the number of TB cases worldwide by 18 millions between 2010 and 2050 [13]. All these findings justify offering smoking cessation interventions in smokers with tuberculosis.

Active smoking increases the severity of pulmonary TB presentation (clinical: cough, dyspnea, tiredness with longer time to recovery; chest X-ray: pulmonary excavations; frequent sputum positivity for acid-fast bacilli at the time of diagnosis and higher probability of sputum cultural positivity after 2 months of treatment that prolonged infectivity) [2,7].

Mechanisms of the effects of smoking on TB infection, disease and treatment

Tobacco smoke impairs the lung defense mechanisms against infection making the patient more vulnerable to infection and susceptible to progression to disease after latent infection [14]. This includes the decrease of mucociliary clearance, phagocytic function of alveolar macrophages and of the activity of natural killer cells; nicotine is involved in a reduced production of proinflammatory cytokines such as TNF- α , IFN- γ , IL-1, IL-6, IL-8, IL-12 [2,14,15]. An impaired immune response in smokers could affect the performance of IFN- γ Release Assays (IGRAs) [16].

Tobacco through induction of cytochrome P 450 enzymes causes lower plasma rifampicin levels in smokers compared to non-smokers [17].

Factors associated with smoking in patients with TB.

A study conducted in units of TB control in Morocco [18] have found after adjusting for confounding variables, smoking and low income (OR= 2.25; 95%CI: 1.06 - 4.76 and 3.23 95%CI: 1.12 - 9.32) significantly associated with treatment failure. In smokers with TB factors significantly associated with treatment default were: being male (OR = 3.2; 95% CI: 1.2-8.7), being a non-religious Muslim (OR = 2.0; 95% CI: 1.4-2.9) and living in an urban area (OR = 3.0; 95% CI: 1.8-4.9) [19]. In Spain, smokers with TB are more frequently homelessness with harmful habits: Alcoholism, use of injected drugs compared to non-smokers [20].

Tobacco smoking increases the risk for progression of Latent Tuberculous Infection (LTBI) to TB (OR/RR=2-3) [21], smokers are less compliant with medications than non-smokers [22]. These findings must be considered before initiating preventive

treatment of LTBI. The treatment may avoid future cases of tuberculosis but effectiveness of preventive treatment depends in a large part on treatment completion. A study conducted in Switzerland in a population of asylum seekers with positive IGRA has not clearly identified smoking as associated factor with LTBI [23] but that a short course of treatment well monitored with stable housing conditions allow a high rate of preventive treatment completion [24].

Smokers have a lower body mass index at the time of the diagnosis of TB [7] which seems to account for a more advanced disease, a diagnosis of the disease or a use of care late..

Helping smokers with TB to stop smoking

Benefits of stopping smoking in TB patients

Active smoking is an independent risk factor of TB treatment failure [2]. Smokers with TB are receptive to advice to quit but often they start smoking again, justifying cessation intervention associated with the directly-observed treatment (DOT) [3,7].

Several studies conducted in developing countries have demonstrated that compared with TB smokers only cared by Directly-Observed Treatment (DOT), the combination of DOT with brief advice [25] or brief advice and Nicotine replacement therapy [26] or Bupropion [27,28] increases the abstinence rate at the end of the follow up (6-12months). At the end of the TB treatment (6 months) there were significantly lower rates of treatment default and failure in patients with the combination of TB and smoking treatments and a greater improvement of quality of life in quitters [25-26]. Helping smokers to quit smoking may have an important impact on the incidence of TB in developing countries.

Smoking cessation interventions in patients with TB

The WHO Framework Convention on Tobacco Control (WHO FCTC) [29], adopted by the world assembly in 2003 set standards and guidelines for interventions to reduce the demand for tobacco and interventions to reduce tobacco consumption, exposure to tobacco smoke and nicotine addiction. The WHO FCTC has been ratified by 168 countries engaging them in tobacco control

A recent meta-analysis concluded that there is a lack of high-quality evidence, about the effectiveness of cessation interventions in improving TB treatment outcomes [30] However, smoking cessation interventions are not complicated, nor time-consuming; professional interventions may be recorded on the TB treatment file [20]. There are several modalities: The brief advice to stop smoking, the following five steps called 5As (Ask about tobacco use, Advise to quit, Assess willingness to make a quit attempt, Assist in quit attempt, Arrange follow up) approach that facilitates counseling, cognitive and behavioral strategies to reinforce the motivation to quit smoking and the ability to control craving; in patients with high level of tobacco dependence, medication treatments (nicotine replacement therapy, bupropion, and varenicline), effectively decrease withdrawal syndrome and craving [21].

Barriers to smoking cessation in patients with TB

Pursue DOTS expansion and enhancement, increasing of financing and human resources to undertake DOTS tasks, improving health care services and the access to medication treatments and providing a social support to patients with TB are bases of TB control to which tobacco control must be associated

[4-5].

The announcement of the diagnosis of tuberculosis seems to be a 'teachable moment' to advise to quit smoking and start quitting, the DOT is an effective way to support stopping smoking in smokers suffering from TB but a professional training effort for a better management of smoking cessation in smokers must be done [3,7] In Morocco, the smoking cessation management of respiratory physicians implicated into the national anti-TB program has been evaluated [33] A questionnaire was administered using a phone interview found that more than 84% inquired about the smoking habits of their patients, 70,7% highlight the benefits of stopping smoking but only 5.3% believed that they were well trained to help smokers to stop. A study was conducted in two TB clinics in Rio de Janeiro [34] to determine whether DOTS workers could be trained to deliver smoking cessation counseling and referral interventions in smokers with TB in a 1-day training cessation program. The evaluation 3 months after program completion has shown a improved self-rated efficacy but the ability to help smoking cessation was not reported.

The smoking cessation medications remain too expensive for use in a large scale in developing countries [7].

The prevalence of tobacco smoking among smokers with TB is high. Active and passive smoking are risk factors for mycobacterium tuberculosis infection and progression of latent TB infection to active TB These findings justify the involvement in smoking cessation interventions of healthcare professionals engaged in the management of TB.

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