Smoking and the risk of TB treatment failure

Graham Cope explains why smokers are at greater risk of pulmonary infection, including tuberculosis (TB), and how when they are infected tend to have poorer treatment outcomes

Tuberculosis (TB) continues to be a national as well as a global threat. There were 7892 new cases of TB in the UK in 2013 and an estimated 9 million cases and 1.5 million deaths worldwide (World Health Organization (WHO), 2014). In the UK almost three quarters of TB cases occur among people born outside the UK; with only 15% of these being recent migrants. The majority of cases are concentrated in the most deprived populations; especially among the unemployed, many of whom have known risk factors including alcohol or drug misuse, homelessness or imprisonment (Public Health England (PHE), 2014).

While the major drivers of the TB epidemic in the last two decades, especially at a global level, have been the spread of HIV/AIDS (Falzon et al, 2015), one other important risk factor has emerged which has a significant impact on the risk of infection, the progression from latent to active disease, as well as treatment efficacy, and that is tobacco smoking (Zellweger et al, 2015).

Working alongside specialist nurses, who support patients with their TB treatment, practice nurses are well placed to provide support for smoking cessation. Following suitable training in communication skills and the use of pharmaceutical aids they can provide very brief advice or more intensive motivational interviewing, which are both cost effective approaches to improving smoking cessation (van Rossem et al, 2015).

Smoking and tuberculosis

Nearly 80% of the world's 1 billion smokers live in countries of high TB prevalence. Smoking has profound effects on the respiratory system, being a major risk factor for chronic inflammation leading to chronic obstructive pulmonary disease (COPD) and carcinogenic factors increase the likelihood of lung cancer. But smoking also has important immunosuppressive effects, such that smokers are at significant greater risk of pulmonary infection including influenza and pneumonia.

Cigarette smokers are more easily infected with *Mycobacterium tuberculosis* and are more likely to be diagnosed with the latent form of the disease. Smokers also have a poorer treatment outcome (Yen et al, 2014), with anti-tuberculosis drug treatment being more likely to be less effective and the patient is more likely to remain persistently smear positive (Siddiqui et al, 2010), with consequential increased morbidity and mortality (van Zyl Smit et al, 2010).

Smoking has been shown to be associated with more extensive pulmonary TB, with greater lung cavitation and positive sputum smear and culture at baseline. Even in self-declared ex-smokers sputum smears and cultures are significantly more likely to remain positive after 2 months of treatment and less likely to achieve cure or treatment completion within 2 years (Leung et al, 2010).

Consequently, almost one fifth of unsuccessful treatment outcomes can be attributable to smoking, and the key factor appears to be more frequent treatment default. Among successful treatment completers, there was a clear gradient of relapse risk from never-smokers to ex-smokers and current smokers. The treatment default rate is higher among current smokers—double that in never smokers (Lavigne et al, 2006). The high level of risk-taking personality among many smokers is thought to be a major contributory factor (Oni et al, 2012), and this raises major concerns over the emergence of drug resistance and secondary spread within the community (Leung et al, 2015).

Even among those who successfully complete their treatment there is still a substantial increased risk for developing recurrent active TB than the general population. Passive smoking has also been shown to increase the risk of both TB infection and disease (Lueng et al, 2010).

Patients who continue to smoke therefore pose a risk not only to themselves, but also to every other person exposed to their infection and to their cigarette smoke. The situation is expected to be even worse for drug-resistant TB, as the effect of smoking is probably compounded by the generally poorer response to available drugs (El Mahalli and Al-Qahtani, 2015).

Also of importance is that smokers have a

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much higher frequency of loss to follow-up, which is a worrying sign, again probably attributable their personality traits, such that smokers will remain untreated and therefore still propagate TB in the community. As such, the impact of smoking is not only a concern to the individual smoker and their families, but to society as a whole (Leung et al, 2015).

Mechanisms involved

Cigarette smoking has many deleterious effects on the human body, with a series of toxins and carcinogens, but an emerging aspect of smoking is the direct effect of nicotine on the immune system, changing the numbers and ratio of the different leukocytes, with a suppressive action, with reduced cytokine production and pathogen eradicating ability (Andreoli et al, 2015).

This impaired immunity increases the smokers' susceptibility to a number of pulmonary infections (Hocking and Golde, 1979). Cigarette smoke impairs the immune response to bacteria by reducing their clearance, impairing elimination of dead and dying cells, and reducing cytokine production (Feldman and Anderson, 2013).

Smokers tend to have more alveolar macrophages than non-smokers; but these cells appear to have sub-optimal function and activity (Karimi et al, 2012). This is likely to be because of reduced synthesis of specific cytokines, notably tumour necrosis factor, interferon and interleukin-1b. Tobacco smoking also impedes the pulmonary function of anti-TB T-helper cells by inhibiting the innate immune activation and lung T-cell recruitment (Shaler et al, 2013). Therefore, the pulmonary compartment has a number of immune impairments that provides some explanations as to why cigarette smoking renders a patient susceptible to tuberculosis infection and disease (O'Leary et al, 2014).

These effects are probably a direct consequence of nicotine acting on specific receptors on the membranes of these immune cells, affecting their activity and interaction with other immune cells, reducing their overall activity (Chan et al, 2014).

Smoking cessation

Smoking cessation is therefore a priority in all TB patients who smoke, to protect the individual patient, their health professionals and the general community (Leung et al, 2015).

'Making Every Contact Count' is an initiative that aims to improve health by encouraging health professionals to inspire lifestyle changes at every contact with the intent to maintain or improve the patient's mental and physical health and wellbeing, whatever their specialty or the purpose of the contact (NHS, 2014). Discussing smoking cessation at routine TB appointments is an example of this.

The first major obstacle to implementing smoking cessation initiatives is to correctly identify those who smoke. There is growing evidence that there is a high rates of denial of smoking among TB patients when questioned by health professionals, with 24% of tobacco users failing the declare their tobacco use prior to biochemical verification (Carver et al, 2014).

With areas of high TB prevalence being in resource-poor regions, and because of the relative recent emergence of smoking as a risk factor for tuberculosis, the number of published studies on the impact of smoking cessation on the outcome of tuberculosis is relatively low. Smoking cessation is frequently overlooked as a priority in this population, with barriers being insufficient time, lack of specific training and inadequate resources for pharmaceutical aids, yet significant effects can be achieved cheaply with relatively little staff training. Staff can deliver quick, effective advice to stop smoking and this can reduce the burden of smoking on TB.

Most of the published findings relate to smoking cessation programmes in countries with a high TB burden, but the same approach has applications here in the UK. One study conducted in Sudan clearly demonstrated that tuberculosis patients who were cared for by health workers who had been minimally trained in smoking counselling had a better outcome than those who were not treated in this way. Advice and information about tobacco smoking and the use of smokeless tobacco was included along with usual care (El Sony et al, 2007).

Brief advice on smoking cessation was also given to patients starting anti-tuberculosis treatment in the National Tuberculosis Programme setting in Eastern Nepal. The intervention took just a few minutes and was repeated after 2 and 5 months after initiation of treatment. The programme followed the format of the 5 A's (Fiore, 2000):

- Asking the patient about their smoking status
- Assessing their willingness to make a quit attempt

- Advising them to stop smoking
- Assisting them with practical steps in their efforts to stop
- Arranging for follow-up visits.

This approach led 39% of patients to biochemically verified quitting for least 6 months. This study showed that brief smoking cessation advice can be incorporated into resource-poor settings and that it should become a mandatory component of any national tuberculosis programme (Campbell et al, 2014).

Motivational interviewing is a longer, more resource demanding approach to smoking cessation, and involves a sympathetic, listening and advising attitude by the smoking cessation counsellor, who tries to understanding the thoughts and motivations of each patient in their behavioural and lifestyle choices and attitudes to change (Lundahl et al, 2013). Such an approach was used in a number of South African townships and found to successfully achieve a biochemically verified 6-month sustained abstinence—double that of usual care. The investment in specific training, with time allocated for intensive behavioural counselling, was deemed to be cost-effective in the long-term (Louwagie et al, 2014).

Incorporating smoking cessation into a direct observation of therapy (DOT) programme has also proved successful, with DOT providing a 'teachable moment'. This approach was implemented in Malaysia with participants receiving individualized behavioural therapy along with practical advice about drug ingestion, and this achieved impressive smoking cessation rates at both 7-day point prevalence and 6-months continuous abstinence. Furthermore, at the end of TB treatment there were significantly lower rates of treatment defaults and treatment failures in the intervention group. The successful quitters also had a better health-related quality of life than those who received the usual TB care (Awaisu et al, 2012).

The incorporation of nicotine replacement therapy (NRT) into the cessation programme has been shown to double quit rates over placebo (Mills et al, 2012), yet this approach is not generally available in most high-burden TB areas. In the UK NRT is widely available, with combinations of slow release formulae such as patches being used together with rapid release formulae, such as gum, lozenges or nasal sprays to provide a quick relief of nicotine withdrawal symptoms when needed (Shahab et al, 2013). NRT when used with behavioural counselling has been shown to double or even more the quit rates of patients with TB who were willing to consider abstinence from tobacco and set a quit date (D'Souza et al, 2012).

Conclusions

Considering the negative impact of smoking on the infection and transmission of tuberculosis, and the potential gains associated with cessation, it is a clear duty of all health professionals managing tuberculosis patients to address this important issue with their patients. Smoking continues to be the most important cause of preventable morbidity and mortality. Correctly identifying smokers then providing very brief advice with follow-up and, if resources allow, more intensive motivational interviewing with pharmaceutical aids to alleviate nicotine withdrawal will have a significant impact both on reducing disease progression and the efficacy of antimicrobial treatment. Strengthening measures for the control and prevention of tobacco smoking may have an additional and welcome impact on our progress towards tuberculosis elimination (D'Ambrosio et al, 2013).

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KEY POINTS

- Smoking increases the risk of tuberculosis
- The use of tobacco reduces the efficacy of drug treatment
- Smokers more frequently do not complete their treatment
- Many with TB deny smoking
- Practice nurses can play a role in smoking cessation

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