Supplements for Smoking-Related Lung Diseases

Subjects: Pathology

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Supplements for smoking-related lung diseases are considered as nonfood products and thought to improve health. Multivitamins and antioxidants are the most commonly dietary supplements used by cancer and asthma patients. There are currently no clear regulatory guidelines that include dietary supplements and their effect on lung cancer and asthma patients, particularly in smokers. Several countries have taken steps to overcome challenges in regulating dietary supplements in the marketplace. These challenges include inadequate assurance of safety/efficacy, inaccuracy of product labeling, misleading health claims, and lack of analytical techniques for dietary supplements. There is a need to establish standards and regulation of dietary supplement use in patients with lung cancer and asthma. The aim of this entry is to expand knowledge on dietary supplements use and smoking-related lung diseases (lung cancer and asthma).

Keywords: asthma ; lung cancer ; supplements ; smokers ; nonsmokers

Smoking is known as one of the main causes of lung cancer and the most common cause of cancer mortality in men and women worldwide [1]. It has been estimated that around 7 million global deaths per year were caused by smoking [2][3][4]. Cigarette smoke is comprised of thousands of chemical compounds, most of which are toxins [5]. Lung cancer is classified into small cell lung cancer (SCLC) and non-small-cell lung cancers (NSCLCs), with the latter accounting for 85% of lung cancer cases, which is divided into three common subtypes-associated smoking, including large-cell carcinoma, squamous-cell carcinoma, and adenocarcinoma [6]. Reviews of published systematic reviews and meta-analyses have confirmed that the risk of lung cancer is increased in current and former smokers [7][8][9][10][11]. In fact, tobacco smoke is the largest contributor to adenocarcinoma and small-cell and squamous cell carcinoma, with over 76% of lung cancer deaths in men and 37–42% of lung cancer deaths in women aged ≥50 years attributable to tobacco use [12]. The link between smoking and lung cancer risk varies significantly by sex. A number of systematic reviews and meta-analyses examined the sex differences in smoking-related risk of lung cancer. One previous systematic review and meta-analysis showed that currently smoking men had higher susceptibility to lung cancer than women [13]. In a recent meta-analysis, currently/formerly smoking men and women had an increased risk of lung cancer, with no significant sex differences observed [14]. Another recent meta-analysis showed that passive smoking/secondhand smoking (SHS) increased the risk of lung cancer in nonsmoking women [15]. A few studies that have examined the sex differences in histological types of lung cancer have shown that lung adenocarcinoma incidence was higher in women than in men [16][17]. Although a declining prevalence of smoking among women was noted, the risk of mortality from smoking continues to rise [18].

Epidermal growth factor receptor (EGFR) mutations have emerged as a key player in lung tumor development. EGFR stimulates two main downstream signaling pathways; the phosphoinositide 3-kinase (PI3K) and the Ras–Raf–mitogen-activated protein kinase kinase (MEK)–mitogen-activated protein kinase (MAPK) [19]. Kirsten rat sarcoma viral oncogene homolog (KRAS) is identified as the most predominantly mutated oncogene, with mutations occurring at codons 12 and 13 in NSCLCs [19], particularly among smokers rather than nonsmokers in patients with lung adenocarcinoma [20][21], and affects cellular processes, including tumor angiogenesis, gene transcription, and cell proliferation [22][23][24]. By contrast, the tyrosine kinase (TK) domain mutations of the EGFR gene are more frequently found in patients with lung adenocarcinoma in nonsmokers than in smokers [25]. Deregulation of EGFR signaling in all histological types may contribute to lung pathogenesis. In fact, aberrant EGFR signaling pathways in most NSCLCs are activated by stimulating EGFR gene mutation, enhancing receptor–ligand binding and increasing the EGFR gene copy number via polysomy/amplification [23][24].

Asthma is one of the major prevalent chronic inflammatory diseases among young adults, the prevalence of which has been shown to be higher in developed countries than developing countries [26], and higher in females than males [27]. Asthma mortality rates were lower than other chronic diseases [28]. However, asthma mortality rates increased with increasing age, and the highest mortality rate was seen in adults aged 65 and over [29]. Asthma mortality data reported that the Netherlands and South Africa had the highest asthma mortality rate globally [26]. Adult-onset asthma may increase the risk of comorbid conditions such as dyspepsia, fluid and electrolyte disorders, chronic obstructive pulmonary disease (COPD), hypertension, congestive heart failure, and diabetes [30].

Asthma is characterized by airway hyperresponsiveness, which results in episodes of shortness of breath (dyspnea), coughing, chest tightness, and wheezing [31]. The type 2 immune responses (Th2) are associated with asthma and mediated by IgE-producing B cells, basophils, type 2 innate lymphoid cells (ILC2s), cytokines, mast cells, and eosinophils [32][33]. A number of environmental factors, including smoking, are associated with the development of asthma in children and adults [34]. Tobacco smoking is reported to cause nearly 10% of asthma mortality worldwide [12]. Tobacco smoke provokes asthma exacerbations and causes other allergy symptoms to worsen in adults [34]. There is also unequivocal evidence that SHS exposure is the main contributor to asthma and lung cancer risk in nonsmokers, disproportionately affecting women [7]. Smoking is able to trigger Th2 inflammation and increase the production of pro-inflammatory cytokines, including interleukin (IL)-4, IL-5, IL-6 IL-13, IL-17A, interferon-γ (IFNγ), and tumor necrosis factor α (TNF-α) [34]. A few studies showed higher levels of total immunoglobulin E (IgE) [35][36], sensitive C-reactive protein (hs-CRP), and malondialdehyde (a marker of oxidative stress) [36], in current and passive smokers than never-smokers. Other studies showed increased white blood cell (WBC) counts, and blood monocytes, lymphocytes, neutrophils, and leukocytes in current smokers in comparison to nonsmokers [37][38]. Cigarette smoking stimulates nasal epithelial cells, resulting in increased lipopolysaccharide (LPS) binding, neutrophil chemotaxis, Toll-like receptor (TLR) 4 expression and reactive oxygen species (ROS) production [39]. Cigarette smoking has shown to decrease CD83+ (a surface expression for mature dendritic cells) counts in smoker patients with asthma [40].

Dietary supplement use among adults is rising, but there is a substantial heterogeneity between supplement users depending on the type, consumption frequency, duration, and reason for supplements used [41][42][43]. Dietary supplement use differs by lifestyle and sociodemographic factors and geographical location among adults [44][45][46][47]. Supplement use also varies according to smoking status. Previous studies have shown that ex-and nonsmokers are more likely to be users of supplements than current smokers [45][46].

There is controversy over the role of dietary supplements in reducing or treating lung cancer in smokers and nonsmokers. There is also much uncertainty about its effectiveness and the consequences in asthmatic smokers and nonsmokers, and our understanding of whether dietary supplements can reduce lung cancer risk in asthmatic smokers and nonsmokers remains unclear in the absence of clinical trials [48]. In order to evaluate the safety and effectiveness of dietary supplement use by asthmatic smokers and nonsmokers before, during, and after lung cancer treatment, realistic and reliable studies worldwide are needed.

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