

E-cigarette or Vaping Product Use-Associated Lung Injury (EVALI): a review

E-cigarette or Vaping Product Use-Associated Lung Injury (EVALI): uma revisão

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ABSTRACT

This study proposes to review the available scientific literature on EVALI, to discuss its epidemiology, clinical features, diagnosis, and treatment of the disease. For this, the PubMed database was accessed, using the following descriptors: "EVALI", "E-Cigarette", "Acute lung injury", "Respiratory failure", "Vaping" and "Juuling". Epidemiologically, the disease is more frequent in young male adults, and high rates of associated psychiatric illnesses have been observed in studies in this population. Clinically, EVALI presents non-specifically, mainly with respiratory and gastrointestinal symptoms, being diagnosed with a history of vaping in the last 90 days, consistent radiological findings and exclusion of other diagnoses. Treatment is similar to other forms of respiratory failure, with oxygen therapy and ventilatory support if saturation <95, in addition to early treatment with corticosteroids and antimicrobial therapy. Due to the non-standardization of electronic cigarettes and the recent identification of the disease, further studies are still needed to establish more specific guidelines for its diagnosis and treatment.

Keywords: Vaping. Smokers. Electronic Nicotine Delivery Systems.

RESUMO

Este estudo propõe a revisão da literatura científica disponível sobre EVALI, para discutir a sua epidemiologia, características clínicas, diagnóstico e tratamento da doença. Para tal, foi acedida a base de dados PubMed, utilizando os seguintes descritores: "EVALI", "E-Cigarette", "Lesão pulmonar aguda", "Falha respiratória", "Vaping" e "Juuling". Epidemiologicamente, a doença é mais frequente em jovens adultos do sexo masculino, tendo sido observadas elevadas taxas de doenças psiquiátricas associadas em estudos nesta população. Clinicamente, EVALI apresenta não especificamente, principalmente com sintomas respiratórios e gastrointestinais, sendo diagnosticada com um historial de "vaping" nos últimos 90 dias, resultados radiológicos consistentes e exclusão de outros diagnósticos. O tratamento é semelhante a outras formas de insuficiência respiratória, com oxigenoterapia e suporte ventilatório se a saturação <95, além de tratamento precoce com corticosteróides e terapia antimicrobiana. Devido à não padronização dos cigarros eletrônicos e à recente identificação da doença, são ainda necessários mais estudos para estabelecer directrizes mais específicas para o seu diagnóstico e tratamento.

Palavras-chave: Vaping. Sistemas Eletrônicos de Liberação de Nicotina. Tabagismo.

INTRODUCTION

Since 2014, a new tobacco product, electronic cigarettes, has been widely used by the young population, especially teenagers, which has brought great concern to pulmonologists^[1,2]. This new product consists of an electronic device designed to vaporize chemical compounds, whether or not they contain nicotine^[3]. Depending on the model, the use of these devices is called vaping or Juuling^[4].

Late effects still remain unknown, due both to the lack of manufacturing standards, making it difficult to predict pulmonary exposure for the generic class of e-cigarettes, and to the relatively recent introduction of the device to the market^[5]. However, even though they are sold as a safer alternative to conventional tobacco products or as a transition for individuals who wish to quit smoking^[6,17], the early consequences of the use of these devices have been observed and there are already reports of fatal cases of acute respiratory failure triggered by these devices^[8-10].

The first report of significant lung disease from vaping was in 2019 in the United States^[11]. The term EVALI (E-cigarette or Vaping product use-Associated Lung Injury) was introduced shortly afterwards, simultaneously with the increase in the number of cases of the disease^[12]. In this sense, the present study aims to review the available scientific literature on EVALI.

METHODOLOGY

This is a descriptive and exploratory study, a narrative review of the literature, including studies that address EVALI. For this, the PubMed database was accessed, using the following descriptors: "EVALI", "E-Cigarette", "Acute lung injury", "Respiratory failure", "Vaping" and "Juuling". We also included relevant studies found in the reference list of selected studies.

EPIDEMIOLOGY

Patients with EVALI are mostly young adult males^[13]. In 2020, a multicenter study analyzed 2558 non-fatal and 50 fatal cases of the disease, noting a predominance of men in both categories (67% and 53%, respectively). Age, on the other hand, showed divergence between the categories: 78% of non-fatal cases were in individuals under 35 years of age, while 73% of fatal cases were in individuals over 35 years of age. In addition, both groups had high levels of psychiatric disorders (41% and 65%), indicating a possible risk factor for e-cigarette use^[14].

PATHOPHYSIOLOGY AND CLINICAL PRESENTATION

As mentioned above, as there is no standardization of substances present in these devices, there is no absolute mechanism for all of them. However, devices with nicotine have mostly propylene glycol (PG) and glycerol (GLY), substances known for their irritating characteristic of the respiratory tract, leading to obstruction and inflammation^[15-17]. In addition, PG and GLY do not cross biological membranes and may induce a state of hyperosmotic stress, leading to the secretion of pro-inflammatory cytokines in the lung^[18-20]. This mechanism can activate inflammatory cascades that result in surfactant disturbance and small airway collapse, modifying ventilation/perfusion regulation and thus interfering with gas exchange^[21]. Furthermore, nicotine, present in more than 90% of e-cigarettes, can cause bronchoconstriction of the large airways when inhaled^[22].

Few patients diagnosed with EVALI underwent lung biopsy, but the histopathological findings are consistent with acute lung injury such as acute fibrosing pneumonia, diffuse alveolar damage, and foamy macrophages^[23]. In addition, CDC researchers have already identified Vitamin E acetate in the bronchoalveolar lavage of patients with EVALI as a possible factor of disease severity. The proposed mechanism is the disruption of alveolar surfactant, leading to a decrease in surface tension, alveolar collapse and lung injury^[24].

Classic clinical findings consist of nonspecific respiratory symptoms such as shortness of breath, chest pain, cough and/or hemoptysis. Most patients also report gastrointestinal symptoms such as nausea, vomiting and/or diarrhea and constitutional symptoms such as fever, chills, weight loss and fatigue^[25]. Werner *et al.*^[14] observed a lower incidence of gastrointestinal symptoms in fatal cases than in non-fatal cases (53% and 80% respectively), indicating a greater severity of the disease in the predominantly respiratory form. Laboratory findings are also nonspecific, with an elevation of leukocyte count and erythrocyte sedimentation rate being present^[25].

DIAGNOSTIC AND IMAGING EXAMS

According to the CDC, the diagnostic criteria for EVALI are: history of *vaping* within the last 90 days, consistent radiological findings, and ruling out infection and other differential diagnoses. However, some pulmonologists include bronchoscopy, bronchoalveolar lavage, and lung biopsy^[26].

In general, EVALI presents nonspecific findings on imaging tests. The most frequently reported findings are bilateral ground-glass opacities with areas of consolidation, often with a peculiar pattern of subpleural sparing and the presence of a reverse halo sign^[25] (Figure 1).



Figure 1. Chest CT of patients with EVALI. In both, symmetrical and bilateral ground-glass opacities with subpleural sparing (arrows) and reverse halo signs are observed bilaterally (arrowheads). In the image on the left, an additional pneumomediastinum (asterisk) is observed^[27].

Imaging findings usually bring a differential diagnosis that includes infection and a variety of patterns of acute lung injury, including pneumonia and diffuse alveolar damage. The main imaging findings and the corresponding lung injury are summarized in (Table 1).

In a multicentric cohort, Kligerman *et al.*^[28] analyzed chest tomography (CT) scans of 160 patients with EVALI. In this study, most patients had a predominantly ground-glass symmetric lung lesion, with the level of consolidation proportional to the severity of the lesion ($p < 0.033$). According to the imaging findings, ninety-seven and a half percent (97.5%) of the patients were classified into the following patterns: diffuse alveolar damage, acute eosinophilic pneumonia, diffuse alveolar hemorrhage, diffuse parenchymal pneumonia, upper lobe pneumonia, and mixed pneumonia.

In addition, a significant difference was observed in the presence of peribronchovascular preservation in relation to the qualitative severity of lung injury on CT ($p < 0.007$), with less preservation in those with a milder form of the disease. Compared with those without, patients with preservation were significantly younger ($p < 0.016$). Other patterns observed were interlobular septa thickening (50.6%) and crazy-paving pattern (18.8%). Interlobular septa thickening, pleural effusion and lymphadenopathy were also associated with lesion severity ($p < 0.013$, $p = 0.016$ and $p = 0.007$, respectively).

TREATMENT

According to CDC recommendations, patients with suspected EVALI and saturation $< 95\%$ in room air should be hospitalized, with oxygen therapy and ventilation support, such as invasive mechanical ventilation, in a protective strategy, similar to that used in acute respiratory distress syndrome (ARDS)^[29].

Table 1. Main presentations of EVALI on chest tomography.

Image finding	Type of lung injury
Bilateral ground-glass changes in the upper and middle zones, with thickened perihilar bronchial wall and presence of secretion in the airways	Hypersensitivity pneumonitis
Manifestation of tree-in-bud patterns in both lungs with subpleural sparing	Bronchiolitis obliterans
Bronchial wall thickening with bilateral centrilobular infiltrate, diffuse ground-glass opacities consistent with diffuse alveolar hemorrhage. Presence of air bronchogram, pleural effusion, and peribronchial ground-glass opacities in the upper and middle lobes	Nonspecific EVALI
Diffuse ground-glass opacities and bilateral subpleural cysts	Lipoid Pneumonia
Hilar lymphadenopathy, fibrotic areas, and ground-glass opacity	Pneumonia por intoxicação

As with other causes of respiratory insufficiency, EVALI is treated early with corticosteroids and antimicrobial therapy^[12]. Corticosteroids were the treatment of choice in most case series, with satisfactory results^[30]. There are still no recommendations for doses and duration of treatment, with discharge only if clinical stability is guaranteed^[29].

CONCLUSIONS

EVALI is a recent pathology with a nonspecific clinical presentation, being diagnosed mainly through a recent history of vaping and radiological exams with consistent findings.

Therefore, with the increasing use of electronic cigarettes, EVALI becomes an important etiology to be considered in cases of respiratory failure, especially among young people. However, the scientific literature is still limited by the non-standardization of these devices, making it impossible to identify all the substances involved in the pathophysiology of the disease.

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