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Impact of habitual marijuana and tobacco smoke on severity of chronic rhinosinusitis

Osama G. Abdel-Naby Awad

Otolaryngology, Head and Neck Department, Minia University Hospital, 122 Kornish El-Neel Street, Minia City, Minia 61111, Egypt

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ABSTRACT

Purpose: Health concerns around cannabis (marijuana) use have focused on the possible relationship with psychosis and lower airway health, however; the effect of cannabis smoking on upper airway health has received less attention. The aim of this study is to investigate difference between exclusive tobacco cigarettes smoking compared with tobacco plus cannabis smoking regarding severity of chronic rhinosinusitis (CRS).

Material and methods: A prospective cross-sectional study with two groups of CRS patients recruited (Group 1: tobacco cigarettes smokers; 100 patients and group 2: tobacco cigarettes smokers and also cannabis users; 100 patients). Recruitment occurred in a general practice in Egypt. Cannabis use was recorded by self-report. Severity of CRS was assessed and compared between 2 groups using SNOT-20 questionnaire, Lund-Mackay CT score and Lund-Kennedy (LK) endoscopy Score.

Results: Group 2 patients (tobacco plus cannabis smokers) had significantly higher mean of assessment cores (SNOT-20 ($P = 0.005$), Lund-Mackay CT score ($P = 0.006$) and Lund-Kennedy (LK) endoscopy Score ($P = 0.005$)). Group 2 patients also had significantly higher mean of facial pain/pressure, difficulty sleep, and wake at night, lack of sleep, wake up tired, fatigue, reduced productivity, reduced concentration, frustration/restless/irritable, sad and embarrassed compared to patients in group 1.

Conclusion: Adult patients who smoked tobacco cigarettes plus cannabis mixed with tobacco had greater health related quality of life burden and more severe CRS compared to patients who smoked tobacco cigarettes only.

1. Introduction

Chronic rhinosinusitis (CRS) represents an important healthcare problem in the world with a significant health and economic impact. CRS is defined as inflammation of the nose and paranasal sinuses. CRS is characterized by two or more symptoms; one of which should be nasal blocking, nasal discharge, facial pain, reduction or loss of smell. These symptoms should be associated with endoscopic signs of polyps and/or mucopurulent discharge together with computerized tomography (CT) changes showing mucosal changes within osteomeatal complex (OMC) and/or sinuses for > 12 months [1,2]. There are numerous proposed etiologies of CRS which include alterations in innate immunity, inflammatory dysregulation, biofilms, and super-antigen effects [3]. As a mechanical and immunologic barrier; sinonasal epithelial cells serve and act as a frontline defense against inhaled pollutants, irritants and toxins. Environmental factors such as allergens and inhaled pollutants such as cigarette smoke may play a significant role in diseases of the upper airway including asthma, otitis media and rhinosinusitis. Second-hand smoke also has its effect on upper airway diseases similar to the effect of active tobacco smoking [3].

Cannabis, commonly known as marijuana, is a product of the *Cannabis sativa* plant with active compounds known as cannabinoids. For several centuries, marijuana has been used as an alternative medicine in many cultures, it has beneficial effects in the treatment of nausea and vomiting associated with cancer chemotherapy; anorexia and cachexia seen in HIV/AIDS patients; and in neuropathic pain and spasticity in multiple sclerosis [4–7]. The discovery of cannabinoid receptors (CB1 and CB2) made important advance in recent years for the investigation of the therapeutic effects of cannabinoids. CB1 expression is predominant in the CNS especially on presynaptic nerves, and CB2 is primarily expressed on immune cells [8,9].

Cannabis is a commonly used substance worldwide, with a United Nations report estimating that 3.9% of the global population uses the drug [10]. The acceptance of its use is growing, 54% of Americans support the legalization of marijuana, up from 17% in 1991 [11]. Medical use of marijuana is supported by 76% of medical professionals [12]. Laws in United States follow this popular opinion, two states legalizing marijuana for adult use and 20 states legalizing its use for medicinal purposes [13]. Given these changes, it is ever more relevant for continued research into the long-term health effects of marijuana

E-mail address: Usama.abdelnabi@mu.edu.eg.

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use.

Although research on marijuana's effects on respiratory health has been conducted since the 1970s, there is still considerable uncertainty and controversy. Health concerns around cannabis use have typically focused on the potential relationship with psychosis. The effect of cannabis use on respiratory health has received less attention and its effect on paranasal sinuses was not discussed adequately in literature. The pulmonary effects of marijuana and tobacco are different; although they have similar amounts of volatile and tar components [14]. Marijuana exposure has an immediate bronchodilator effect followed with increase in airway inflammation and symptoms of chronic bronchitis, however; studies of its long-term effects reported varying results that suggest either no effect or some decrement in lung function [14,15]. The aim of the current study is to examine the effect of marijuana use on objective and subjective assessment parameters of CRS severity compared to exclusive tobacco smoking.

2. Patients and methods

2.1. Recruitment, classification of cannabis and tobacco use

Participants were recruited from patients attending at our private clinic in Minia city, Egypt between May 2015 and September 2018. Individuals aged ≥18 years with current smoking were identified in appointment lists and approached by a researcher who explained the study and determined eligibility. The study was approved by the Committee for Medical Research Ethics in Egypt, 2015NBA5723234. All patients signed a written consent prior to inclusion in the study. No pharmaceutical companies funded the study or contributed to the study design, outcome evaluation or writing of this study.

Individuals were eligible for recruitment if they have CRS based on the criteria of the Academy of Otolaryngology-Head and Neck Surgery Rhinosinusitis Task Force [16], with imaging modalities for confirming the diagnosis of CRS in the form of CT scan demonstrating: diffuse mucosal thickening, bone changes, or air-fluid level with ongoing symptoms consistent with CRS. All included patients had medical treatment for CRS (e.g. antibiotics, topical nasal steroids and nasal saline spray) for variable durations before inclusion in the study.

The study involved 200 patients with CRS classified into two groups. Group 1: included 100 patients with heavy tobacco cigarettes smoking (at least 20 cigarettes per day for at least 5 years) according to *World Health Organization report on the global tobacco epidemic* [17]. Group 2: included 100 patients with heavy tobacco cigarettes smoking as patients in group 1 plus habitual cannabis use (at least one cannabis joint per day for at least 1 year) [18]. Cannabis joint can usually fit about a quarter of a gram, it is hybrid with half amount tobacco and half amount cannabis, hand-rolled by the user with rolling papers with no cigarette filter. Some patients were alcohol drinkers (Intensity of alcohol consumption was assessed according to the National Institute on Alcohol Abuse and Alcoholism) [19]. Individuals were invited to complete a questionnaire for demographic details, general health, tobacco and cannabis use, and self-reported nasal symptoms.

2.2. Exclusion criteria

Patients with the following were excluded from the study: previous sinonasal surgery, determined allergy (Allergic status was defined as presence of at least one positive skin test on a panel of regionally relevant aeroallergens) and/or asthma, aspirin-induced asthma (Aspirin-intolerance was determined by the patient history of worsening upper and/or lower airway symptoms after ingesting aspirin or other non-steroidal anti-inflammatory drugs), marked septal deviation that may cause unilateral or bilateral osteomeatal complex disease [20,21], chronic hypertrophic rhinitis (i.e. inflammation of the nasal mucous membrane marked by hypertrophy of the mucous membrane of the turbinates and the septum) [22], adenoid enlargement, allergic fungal sinusitis, systemic disease such as tuberculosis, sarcoidosis, bronchiectasis, Wegner granulomatosis, immune deficiency disorders and patients with significant (i.e. daily exposure to large volume) occupational exposure to materials known to be hazardous to the sinuses and lungs (e.g. wood dust [23], nickel, chromium VI and cadmium [24]). Patients with illicit drug use other than cannabis were also excluded from the study.

2.2.1. Patients' assessment

Subjective and objective assessment done for every patient during multiple clinic visits after 3 months of medical treatment for CRS, offered by our medical team to patients in their first clinic visit, in the form of antibiotics, topical nasal steroids (Beclomethasone, 500 mg twice a day in each nostril) and nasal saline spray. Patients' assessment included:

1) Subjective assessment of CRS severity: through 20-Item Sino-Nasal Outcome Test (SNOT-20), which is a validated, self-administered, quality of life instrument specific for patients with symptoms of rhinosinusitis [25]. This instrument measures physical problems, functional limitations, and emotional consequences of sinusitis by asking participants to score 20 items. We translated the questionnaire into an Arabic one and the filling of the questionnaires was performed by every patient assisted by the research team. The questionnaire was completed by every patient with the following instructions:
   - Patients rate the severity of their condition on each of the 20 items using a 0–5 category rating system:
     0 = Not present/no problem.
     1 = Very mild problem.
     2 = Mild or slight problem.
     3 = Moderate problem.
     4 = Severe problem.
     5 = Problem as ‘bad as it can be’.
   - -The total SNOT-20 score is calculated as the mean item score for all 20 items ranging from 0 to 5, with higher scores representing greater health related quality of life burden.
   - Mean of every item calculated and compared and total mean SNOT-20 score of 2 groups was calculated and compared.
2) Objective assessment of CRS severity through:
   A) Lund-Mackay CT staging scores: CT scans were ordered after 3 months of medical treatment for every patient and assessed in a blinded manner. The Lund-Mackay CT scoring system was selected for its simplicity and reproducibility [26]. CT examinations were performed in the same institution without using contrast material.
      - Mean score of each group of sinuses was calculated and compared
      - Total mean score of 2 groups was calculated and compared
   B) Diagnostic rigid nasal endoscopy: Rigid nasal endoscopy was performed for every patient after 3 months of medical treatment. Each nasal side and graded according to the Lund-Kennedy (LK) Endoscopy Score [27]. The LK Endoscopy Score consists of five terms (polyposis, discharge, edema, scarring and crusting) graded on an ordinal scale from 0 to 2 for each side. Higher scores indicate worse observed disease. LK score performed by 2.7-or 4.0-mm rigid 0° or wide angle 30° endoscopes using topical decongestant.
      - Mean score of every item was calculated and compared.
      - Total mean score of 2 groups was calculated and compared.

2.3. Statistical analysis

Statistical analysis was performed with SPSS (SPSS Inc., Chicago, Illinois, USA). P values < 0.05 were accepted as significant. Mean differences between 2 groups for the SNOT-20 scores, Lund-Mackay and

Table 1
Characteristics of study subjects:

Characteristic	Group 1 Tobacco smokers (n = 100)	Group 2 Tobacco + marijuana (n = 100)	P value
Age			
19–30 years	30	34	0.534
31–50 years	40	44	
51 + years	30	22	
Sex			
Male	75	80	0.499
Female	25	20	
Age of first smoking tobacco (years)	15 (12 − 31)	13 (12 − 33)	0.546
Duration of cigarette smoking (years)	12 (5–20)	14 (5–25)	0.453
Age of first smoking cannabis	–	18 (16–33)	–
Comorbidities (number of patients)			
DM	18	20	0.342
Hypertension	24	26	
DM + hypertension	10	12	
Tobacco pack-years, mean	32 (7–120)	25 (8–115)	0.324
Cannabis joint-years, mean	–	110 (5–1030)	–
Alcohol consumption (number of patients)			
Mild	5	8	0.432
Moderate	4	6	
None	91	86	

LK endoscopic score were evaluated for statistical significance using the Student t-test for the total sample. McNemar test was used for comparing the qualitative data.

3. Results

In group 1, of the 100 patients, 75% (75/100) were men and 25% (25/100) were women, with an average age of 35.33 years (19–58 years). In group 2, of the 100 patients, 80% (80/100) were men and 20% (20/100) were women, with an average age of 38.08 years (19–60 years). There was no significant difference between both groups with respect to sex, age and symptom duration. Characteristics and comorbidities of study patients are presented in Table 1. There was no significant difference regarding duration of tobacco smoking and the amount of smoked tobacco in 2 groups even after adding amount of tobacco mixed to cannabis joints in group 2 patients (Table 1).

3.1. Difference in CRS severity of 2 groups

3.1.1. Difference in SNOT-20 score

None of 200 patients had any missing values for any of the 20 SNOT-20 items. Mean SNOT-20 score in group 1 was 54.6 which was significantly lower compared to mean score in group 2 which was 70.2 (P = 0.005) (Table 2).

Patients with Marijuana smoke had significantly higher mean of following symptoms: facial pain/pressure, difficulty sleep, and wake at night, lack of sleep, wake up tired, fatigue, reduced productivity, reduced concentration, frustration/restless/irritable, sad and embarrassed (Table 3). However; 2 groups had no significant difference in mean of postnasal discharge, thick nasal discharge, ear fullness, ear pain, dizziness, need to blow nose, sneezing, runny nose and cough

Table 3
Difference in mean of separate items of SNOT-20 score between 2 groups.

Question	Group 1 Tobacco smokers (mean ± SD)	Group 2 Tobacco + marijuana (mean ± SD)	P value
Need to blow nose	4 ± 0.32	3 ± 0.33	0.324
Sneezing	4 ± 0.21	4 ± 0.45	0.876
Runny nose	4 ± 0.12	4 ± 0.65	1.00
cough	4 ± 0.33	5 ± 0.61	0.232
Postnasal discharge	4 ± 0.23	4 ± 0.35	0.981
Thick nasal discharge	3 ± 0.32	4 ± 0.64	0.543
Ear fullness	3 ± 0.33	3 ± 0.65	1.00
Dizziness	2 ± 0.67	3 ± 0.51	0.543
Ear pain	3 ± 0.21	3 ± 0.34	0.867
Facial pain/pressure	2 ± 0.33	5 ± 0.98	0.002*
Difficulty sleep	2 ± 0.43	5 ± 0.99	0.003*
Wake at night	2 ± 0.66	5 ± 0.89	0.002*
Lake of sleep	3 ± 0.23	5 ± 0.39	0.001*
Wake up tired	3 ± 0.77	5 ± 0.86	0.002*
Fatigue	2 ± 0.54	5 ± 0.87	0.001*
Reduced productivity	2 ± 0.87	4 ± 0.67	0.004*
Reduced concentration	2 ± 0.45	4 ± 0.75	0.004*
Frustration/restless/irritable	2 ± 0.54	5 ± 0.99	0.001*
Sad	2 ± 0.64	5 ± 0.73	0.001*
Embarrassed	1 ± 0.12	5 ± 0.79	0.001*

McNemar test for comparing clinical variables.
* Significant difference (P-value < 0.05).

Table 2
Difference of subjective and objective assessment scores of CRS between 2 groups.

	Group 1 Tobacco smokers (mean ± SD)	Group 2 Tobacco + marijuana (mean ± SD)	P value
SNOT-20 score[a]	54.6 ± 3.43	70.2 ± 2.21	0.005*
Lund-Mackay CT score[b]	14 ± 2.67	19 ± 2.34	0.006*
Lund-Kennedy (LK) Endoscopy Score[c]	6 ± 1.54	10 ± 2.34	0.005*

[a] SNOT-20: 20-Item Sino-Nasal Outcome Test (higher scores representing greater health related quality of life burden).
[b] Higher score representing greater sinus affection.
[c] Higher score representing more severe disease.
* Significant difference (P-value < 0.05).

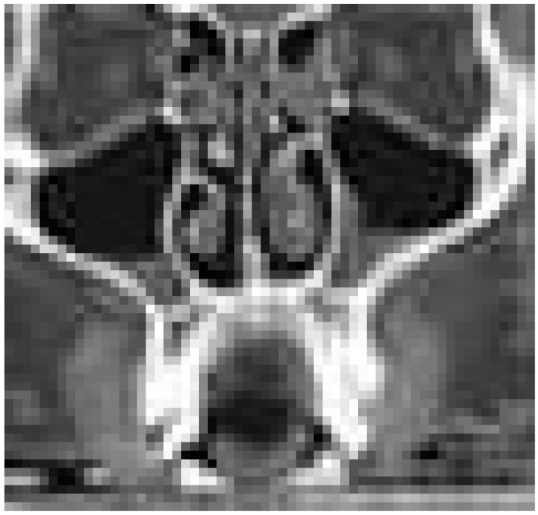

Fig. 1. CT; coronal view of male patient with habitual marijuana and tobacco smoking showing bilateral maxillary and ethmoidal sinusitis with obstructed osteomeatal complex.

(Table 3).

3.1.2. Difference in Lund-Mackay CT staging scores

Marijuana smoke patients had significantly higher mean CT scores compared to tobacco smoke patients (20 vs. 12, respectively, $P = 0.006$) (Table 2).

Patients with Marijuana smoke had significantly higher mean of maxillary, ethmoidal affection and obstruction of osteomeatal complex (Fig. 1). The two groups had no significant difference in mean of frontal and sphenoidal affection (Table 4).

3.1.3. Difference in Lund-Kennedy endoscopic scores

Marijuana smoke patients had significantly higher mean LK endoscopic score compared to tobacco smoke patients (6 vs. 10, respectively, $P = 0.005$) (Table 2).

Patients with Marijuana smoke had significantly higher incidence of thick and purulent discharge and presence of severe edema (Fig. 2). However; 2 groups had no significant difference in incidence of presence of nasal polyps, scarring and crusting (Table 5). Interestingly; one of Marijuana smoke patients has large septal perforations with no obvious cause and another patient has chronic unilateral septal ulcer.

4. Discussion

In our comparative study, we provided the evidence that habitual marijuana use and heavy tobacco smoking are more harmful to paranasal sinuses compared to exclusive heavy tobacco cigarettes smoking. The advantage of using tobacco cigarette smoking as a control group is that it is the most clinically relevant stimulus, which triggers inflammatory pathways leading to sinus inflammation.

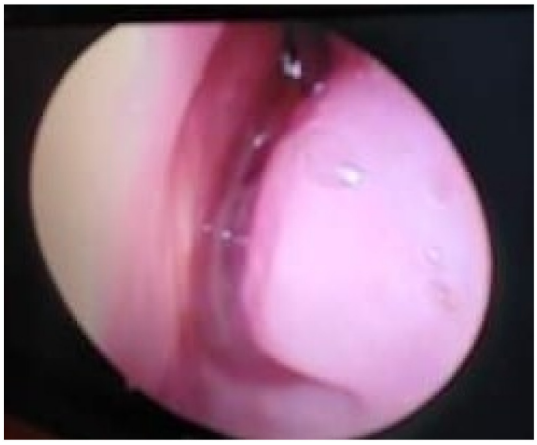

Fig. 2. Endoscopic view; left side of same patient with habitual marijuana and tobacco smoking showing congested mucosa and thick secretions.

Table 5
Difference in mean of separate items of Lund-Kennedy (LK) endoscopy score between 2 groups.

Characteristics	Group 1 Tobacco smokers (mean ± SD)	Group 2 Tobacco + marijuana (mean ± SD)	*P* value
Nasal polyps	2 ± 0.13	2 ± 0.43	0.865
Discharge	2 ± 0.14	4 ± 0.45	0.002*
Edema	2 ± 0.33	4 ± 0.32	0.003*
Scarring	1 ± 0.25	2 ± 0.41	0.345
Crusting	2 ± 0.44	2 ± 0.14	0.923

Higher score representing more severe disease. McNemar test for comparing clinical variables.
* Significant difference (*P* value < 0.05).

There is no strong evidence of deleterious effects of cannabis use on objective measures of respiratory function; although cannabis is associated with greater reported respiratory symptoms [14,28–36], subjects studied in this concern have been relatively young and have almost exclusively used herbal. In countries such as Egypt resin cannabis (known as 'hashish') smoked illegally in a cigarette prepared with tobacco, known colloquially as a 'joint' appears to be the most common form of consumption. During recruitment of patients; we didn't find patients with exclusive cannabis smoking. In a trial to overcome bias of difference in amount of smoked tobacco, we selected patients with heavy tobacco smoking (i.e. with high smoking index) where degree of tobacco exposure is correlated to risk of diseases such as lung cancer [17] in one group compared to patients with heavy tobacco smoking plus habitual cannabis smoking in second group. Cannabis use usually extends into middle adulthood leading to its accumulation after exposure. Effects of such exposure can only be studied in established cannabis users.

Multiple studies have analyzed the pathophysiologic effects of

Table 4
Difference in mean of separate items of Lund-Mackay CT score between 2 groups.

Sinuses	Group 1 Tobacco smokers (mean ± SD)	Group 2 Tobacco + marijuana (mean ± SD)	*P* value
Frontal	2 ± 0.11	2 ± 0.54	0.543
Maxillary	2 ± 0.23	4 ± 0.43	0.004*
Anterior ethmoids	2 ± 0.43	4 ± 0.24	0.003*
Posterior ethmoids	2 ± 0.14	4 ± 0.36	0.003*
Sphenoid	2 ± 0.15	2 ± 0.25	0.675
Osteomeatal complex	2 ± 0.43	4 ± 0.27	0.001*

Higher score representing greater sinus affection. McNemar test for comparing clinical variables.
* Significant difference (*P* value < 0.05).

tobacco smoke on sinonasal mucosa. Tobacco smoke induces nasal response including increased nasal airway resistance, nasal irritation, nasal congestion, rhinorrhea and it has adverse effects on mucociliary clearance and innate immune function of sinonasal epithelium with olfactory mucosal metaplasia [37]. Volume of smoking is an important factor in outcomes. A large study reported that high volume smokers (defined as over 20 cigarettes a day) had statistically significant worse postoperative endoscopy scores than low volume smokers (less than or equal to 20 cigarettes a day) or nonsmokers [37].

The effect of marijuana on upper airway was not studied (up to our knowledge) before, from our results it was clear that marijuana has negative effect on patients with CRS; this effect can be explained by understanding marijuana effect on the lower airway. Short-term bronchodilation was described in response to marijuana primarily through CB1 receptor activation in the lung [38]. Cannabinoid system has in vivo and in vitro regulatory role to the immune system through its immunomodulatory properties and suppression inflammatory response and subsequently attenuate disease symptoms through multiple pathways such as induction of apoptosis in activated immune cells, suppression of cytokines and chemokines at inflammatory sites; these properties made cannabinoids tested in several experimental models of autoimmune disorders such as multiple sclerosis, rheumatoid arthritis, colitis and hepatitis and have been shown to protect the host from the pathogenesis through induction of multiple anti-inflammatory pathways [39]. However; Helyes et al. [40] studied the effect of marijuana in a predictive mouse model; they reported that marijuana smoke induces remarkable bronchial hyperresponsiveness very early after 7 days of the first smoke inhalation compared to 2 months of tobacco smoke, as well as emphysema, severe pulmonary inflammation and tissue destruction, which are Independent of CB1 receptor activation. They also proved characteristic pathophysiological alterations in lower airway with increase of airway reactivity, also reported that after a longer period of time, marijuana markedly increases airway reactivity to muscarinic receptor activation in a CB1-independent manner with a result of severe inflammation as assessed by several histopathological parameters, such as perivascular/peribronchial edema, epithelial irregularity, neutrophil and macrophage infiltration, hyperplasia, atelectasia, and emphysema [40]. These inflammatory reactions were more severe and developed earlier in the marijuana-exposed group than in tobacco-smoking mice [40]. Vascular endothelial proliferation, narrowed, obstructed, and destructed bronchi with desquamated epithelial cells, infiltration fibrosis, massive interstitial lymphocyte and a remarkable loss of the alveolar structure could be seen after 4 months of regular marijuana smoke exposure [40]. This severe inflammatory response after prolonged marijuana use in lower airway could overweight its anti-inflammatory response and logically explain possible upper airway response.

In this study, we studied the cumulative marijuana use with smoking at least one joint daily for a year. Habitual marijuana smoke increases symptoms of bronchitis, respiratory epithelium of conducting airways and bronchoalveolar lavage fluid of habitual marijuana smokers have increased macro- and microscopic signs of inflammation [41–46]. Chemical compositions of marijuana and tobacco, as well as their smoke are basically different; marijuana does not contain nicotine, and tobacco has no cannabinoid derivatives. Also, marijuana smoke contains double concentrations of phenol, acetaldehyde benzanthracene, hydrogen cyanide, naphthalene and ammonia than tobacco [47]. Marijuana has greater inflammatory actions in the airways due to its higher amount of these irritants, possibly through the activation of peptidergic sensory nerves, blood carboxyhemoglobin level was five times higher and the amount of the inhaled tar was three times greater in marijuana smokers compared with tobacco smokers [48].

Patients with marijuana smoke in this study had significantly higher symptoms of psychological and sleep symptom factors of SNOT-20 (i.e. difficulty sleep, wake at night, lack of sleep, wake up tired, fatigue, reduced productivity, reduced concentration, frustration/restless/irritability, sadness and embarrassment). Cohen et al. [49] reported that cannabis users have significant impairment in working memory, inhibition of long-term memory compared to non-cannabis users, also users have been found to experience more anxiety, paranoia, psychoticism and depressive symptomatology compared to non-users [50,51]. These negative effects of marijuana aggravate psychological and sleep symptom of CRS.

In this study; there was no significant difference between the 2 groups regarding the degree of alcohol consumption. A significant portion of patients diagnosed with chronic inflammatory airway diseases report aggravation of airway symptoms after drinking alcohol. It is not clear whether alcohol itself is responsible or nonalcoholic additives are the main cause of these reactions. Generally, it is assumed that in the majority of patients, the non-alcoholic components, such as histamines or sulphites, are the main causes [52]. Prevalence of these reactions increases with increasing disease severity and was highest in NSAID exacerbated respiratory disease (NERD). Furthermore, in CRS with nasal polyps, nasal alcohol hyper-responsiveness is significantly more frequent in more severe and uncontrolled symptomatic subgroups [53]. Although; it is very difficult to do reliable comparative clinical studies due to a range of modifying factors, such as variability in duration, amount, and simultaneous use of both agents. The main limitations of this study were that the study was cross-sectional, which constrained inference of causality. For efficiency; only smokers were recruited, resulting in the absence of a non-smoking group from this population for comparison. For convenience, we selected our patients from individuals attending a general practice. Tobacco and cannabis use were self-reported and was not corroborated biochemically such as using urine toxicology. Biochemical corroboration of tobacco is valid alongside self-report [54,55]. However; the main strengths of this study that it is a general practice-based sample composed of adults with established tobacco and cannabis use. Investigating the effect of cannabis added to tobacco is important for the community, several studies reported that a single marijuana cigarette per day remarkably increases the risk of malignant lung tumors every year, which is comparable with the risk induced by one package of tobacco cigarette [56]. This comparative study provided the first evidence that prolonged marijuana use induced more severe CRS than tobacco use alone. Well-established scientific information regarding the impact of long-standing marijuana smoking on sinonasal mucosa is important to support legal, political and decision-making. These results provide reliable evidence against unrestricted use of marijuana smoking.

5. Conclusion

This study is the first study from Egypt providing data on the potential impact of habitual cannabis resin smoking on the severity of CRS in a general practice population. Study findings indicate that there are some subjective and objective adverse effects of habitual cannabis smoking over exclusive tobacco cigarettes smoking on severity of CRS and this should possibly be included in future health education messages and law regulations.

McNemar test for comparing clinical variables.

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