Transl Clin Pharmacol. 2024 Mar;32(1):52-62
https://doi.org/10.12793/tcp.2024.32.e4
pISSN 2289-0882·eISSN 2383-5427

Translational and Clinical Pharmacology TCP

Original Article

Check for updates

The effects of opium consumption on severity of disease on hospitalized COVID-19 patients in East of Iran, a prospective cohort study

Abdol Satar Pagheh [1], Toba Kazemi [2], Seyed Mohammad Riahi [2], Mohammad karimi [3], Moloud Foogerdi [4], Anahita Arian [2], Shima Heydari [5], Mohammad Yousef Ghoddousi [2], Parisa Vahdati [1], and Mohammad Reza Khazdair [2,*]

[1]Infectious Diseases Research Center, Birjand University of Medical Sciences, Birjand 9717434765, Iran
[2]Cardiovascular Diseases Research Center, Birjand University of Medical Sciences, Birjand 9717434765, Iran
[3]Department of Emergency Medicine, School of Medicine, Urmia University of Medical Sciences, Urmia 571478334, Iran
[4]Department of Emergency Medicine, School of Medicine, Birjand University of Medical Sciences, Birjand 9717434765, Iran
[5]Department of Internal Medicine, School of Medicine, Torbat Heydariyeh University of Medical Sciences, Torbat Heydarieh 9516915169, Iran

Received: Oct 2, 2023
Revised: Jan 17, 2024
Accepted: Feb 15, 2024
Published online: Mar 7, 2024

***Correspondence to**
Mohammad Reza Khazdair
Cardiovascular Diseases Research Center, Birjand University of Medical Sciences (BUMS), Birjand 9717434765, Iran.
Email: khazdairMR@Bums.ac.ir
M.khazdair@yahoo.com

ORCID iDs
Abdol Satar Pagheh
https://orcid.org/0000-0002-1234-6127
Toba Kazemi
https://orcid.org/0000-0002-6204-4514
Seyed Mohammad Riahi
https://orcid.org/0000-0002-3184-2126
Mohammad karimi
https://orcid.org/0000-0001-6454-2747
Moloud Foogerdi
https://orcid.org/0000-0002-5476-4001
Anahita Arian
https://orcid.org/0000-0001-9109-2526
Shima Heydari
https://orcid.org/0000-0002-7682-3084
Mohammad Yousef Ghoddousi
https://orcid.org/0000-0002-8937-1857
Parisa Vahdati
https://orcid.org/0009-0004-6957-6208
Mohammad Reza Khazdair
https://orcid.org/0000-0001-9854-6121

ABSTRACT

There are few theories and little empirical evidence about the bilateral impact of substance use and coronavirus disease 2019 (COVID-19), so a logical and accurate picture of this area is required. We investigated the effects of opium use on severity of disease on hospitalized COVID-19 patients in east of Iran. Demographic and clinical characteristics, vital signs, laboratory tests, mortality rate, type and duration of opium consumption in hospitalized patients who recovered from COVID-19 in the follow-up after 3 months were evaluated. In this study, 60 (20%) participants were the opium user and 251 (80%) were the non-user patients. Based on clinical symptoms, hypertension and systolic blood pressure in opium user were significantly higher than non-user patients ($p < 0.05$). In the laboratory tests, only the level of urea was higher in the opium positive group (37 [26.5–48.5] vs. 32 [23–43], respectively) and the percent of lymphocytes were lower in the opium positive (17 [8.2–25.8] vs. 18.7 [13.85–26.35], respectively). The initial therapies of both opium positive and negative infected patients showed not any significant changes ($p > 0.05$). Among the studied groups, one deceased case with COVID-19 was related to a drug user patient. Although, uses of opium reduced the levels of some risk factors, vital signs at admission and initial therapies during hospitalization in COVID-19 patients but it increased lung and heart diseases. Also, the severity of COVID-19 including hospitalization and mortality were associated with opium consumption.

Keywords: COVID-19; Communicable Diseases; Disease Severity; *Papaver somniferum*; Opium Poppy

Conflict of Interest
- Authors: Nothing to declare
- Reviewers: Nothing to declare
- Editors: Nothing to declare

Reviewer
This article was reviewed by peer experts who are not TCP editors.

Author Contributions
Conceptualization: Pagheh AS, Kazemi T, Riahi SM, Karimi M, Foogerdi M, Arian A, Heydari S, Ghoddousi MY, Vahdati P, Khazdair MR; Data curation: Pagheh AS, Kazemi T, Karimi M, Foogerdi M, Arian A, Heydari S, Ghoddousi MY, Vahdati P; Formal analysis: Khazdair MR; Investigation: Kazemi T, Karimi M, Foogerdi M, Arian A, Heydari S, Ghoddousi MY, Khazdair MR; Methodology: Pagheh AS, Riahi SM; Supervision: Khazdair MR; Writing - original draft: Pagheh AS, Kazemi T, Riahi SM, Vahdati P, Khazdair MR; Writing - review & editing: Khazdair MR.

INTRODUCTION

Papaver somniferum commonly known as the "opium poppy" is an annual flowering plant, in the family Papaveraceae as the principal source of opium and opiate drugs [1]. This plant has been used traditionally for multiple uses including; as an ornamental plant, food and medicine (e.g. morphine). Also, opium has been known for millennia to relieve pain and recorded its use for surgical analgesia for several centuries [2]. The prevalence of opium consumption was declined compared to the increases of the other substance abuse throughout the world, but in some countries including Iran, opium is still the major drug of abuse, 5.3% in general population to 22.5% in some rural areas [3]. A patient was defined as opium user or addict if he/she had been using opium for at least 12 months prior to admission [4]. Also, the most of people in Iran trust on medical doctors in disclosing their confidential health related information. The opium user group were participants who disclosed that they were addicted to opium [5].

Opium has been used traditionally for lowering blood lipids and prevent heart diseases in many societies including the Middle East and in many Asian countries [6]. It has been reported that opiates uses may have cardio-vascular protective effects including, decrease severity of coronary artery disease (CAD), and incidence of fatal myocardial infarction [7]. Furthermore, the results of some studies indicated that opioid receptors and phosphatidyl inositol kinanse was involved in the beneficial effects of opiates [7,8]. The results of a review article showed opium uses reduced systolic blood pressure (SBP), lipid profile, and fasting blood sugar (FBS), while it could reveal toxic effects on the body [9].

Since the emergence of coronavirus disease 2019 (COVID-19) in 2019 from Wuhan city and its rapid global spread [10], the disease has introduced various psychiatric aspects and triggered widespread misconceptions about the preventive effects of opium consumption [11]. Numerous international studies have investigated factors contributing to the severity, morbidity, and mortality of COVID-19 [12,13]. However, the influence of opium consumption remains inconsistently reported, leading to controversies surrounding its impact on COVID-19 morbidity and mortality [14,15]. Societal misconceptions persist, influencing perceptions of the benefits and risks associated with opium consumption in relation to human health and COVID-19 infection [15]. Amidst limited scientific evidence, social media has propagated myths, suggesting protective effects of opium against COVID-19, particularly in mild cases [15]. Traditional beliefs and studies hint at therapeutic effects of opium, offering relief from headaches, earaches, toothaches, and sexual impotence, alongside recognized analgesic, antitussive, hypnagogic, and antidiarrheal properties [16,17].

The onset of COVID-19, along with disruptions in healthcare and social safety nets, compounded by social and economic stressors, intensified the opioid epidemic [18-21]. Recognizing factors associated with COVID-19 mortality is pivotal for risk reduction and appropriate interventions [22]. Hence, comprehensive studies are essential to elucidate the relationship between opium user and mortality in COVID-19 patients. With these considerations, the main goal of this study was to explore the association between opium user and disease severity in hospitalized COVID-19 patients in East Iran.

https://doi.org/10.12793/tcp.2024.32.e4

METHODS

Study population

This prospective cohort study was conducted to evaluate the physical and mental health of hospitalized patients who recovered from COVID-19 in the follow-up periods of 1, 3 and 6 months in South Khorasan Province, East of Iran. At the baseline phase of the study, we obtained patients' information including, address and phone numbers from the Integrated Health System dataset in health centers and contacted them to attend health center with all their medical documents related to the their hospitalization for COVID-19.

The Ethics Committee of the Vice-chancellery for Research and Technology affiliated with Birjand University of Medical Sciences approved the study's protocol (Ethical code IR.BUMS.REC.1399.546). Patients admitted to the study hospital were eligible for inclusion if they meet the following criteria: 1) Patients who were admitted to Vali-Asr hospital as COVID-19 treatment Centre in Birjand city. 2) Confirmed cases of COVID-19 as a positive result on real-time reverse transcription polymerase chain reaction (RT-PCR) assay of nasal and oropharyngeal swab specimens. 3) Consents to be enrolled in the follow-up study and provide all necessary data, blood sample, and the lung spiral computed tomography scan. After obtaining informed consent, experts collected comprehensive data on demographic characteristics, treatment protocols, and vital and laboratory signs during hospitalization. The research team continued to assess relevant laboratory biomarkers and physical function at 1-, 3-, and 6-month intervals post-discharge.

The opium user group is defined by individuals with a continuous history of opium use predating the onset of COVID-19 infection. Exclusion criteria included hospitalized patients with a negative SARS-COVID-2 virus RT-PCR test; individuals younger than 15 years; patients with insufficient recorded data; and those who lacked laboratory findings or lost 6-month follow-up.

Data collection

The required data consisted of epidemiological and demographic data, vital signs at the time of admission, underlying diseases, clinical symptoms, laboratory results, severity of disease, hospitalization days, mortality rate, and information about the history of opium consumption. The values of complete blood count, lactate dehydrogenase, alanine aminotransferase, aspartate aminotransferase, qualitative C-reactive protein (CRP), blood urea nitrogen (BUN), and creatinine were taken after 3 months of follow-up.

Study definitions

Survival time during hospitalization (length of hospitalization) was defined as the interval between admission and demise. Adolescent or adult with clinical signs of pneumonia and the following criteria were diagnosed with severe COVID-19: (a) respiratory rate > 30 breaths/min and (b) SpO_2 < 90% on room air. Moderate illness in patients included clinical signs of pneumonia but no signs of severe pneumonia, including oxygen saturation or SpO_2 > 90% on room air [23].

Statistical analysis

The collected data were described using central and dispersion indicators, such as the mean and standard deviation for quantitative variables, the frequency and percentage for qualitative variables. The independent t-test was used to compare the means of quantitative variables between the two groups if the distribution of variables in both groups was normal; otherwise,

https://doi.org/10.12793/tcp.2024.32.e4

the Mann-Whitney *U* test was employed. In addition, the χ^2 test and Fisher's exact test were utilized to determine the relationship between qualitative variables. All analyses were conducted with SPSS version 23 (IBM Corp., Armonk, NY, USA), and a significance level of 0.05 was considered.

RESULTS

In this study, out of the 670 patients admitted during this period, 314 patients volunteered for follow-up. The remaining patients declined participation, citing unsuitable physical and mental conditions, leading to their exclusion from the study. The frequency of oral use of opium was higher, while inhalation use was lower in male compared female in opium positive COVID-19 patients. The type of opium consumption in male and female COVID-19 patients was showed in **Table 1**. Demographic information of the study participants showed the Mean age and male gender were significantly difference in the opium user compared to the non-user patients ($p < 0.05$). The frequency of hypertension (HTN) and SBP in opium user were significantly higher than non-user patients ($p < 0.01$ and $p < 0.009$, respectively), **Table 2**.

The frequency of diabetes mellitus (DM), diastolic blood pressure (DBP) and FBS were higher, while the body mass index (BMI) was lower in opium user compared to the non-user patients that these changes were not significant, **Table 2**.

The results about medical history of the current study showed the frequency of heart and lung disease were significantly higher in opium user compared to the non-user patients ($p < 0.05$ and $p < 0.001$), respectively. Although, the frequency of kidney disease, hospitalization days the overall mortality were also higher in opium user compared to the non-opium user patients, but these changes were not significant differences, **Table 3**.

Table 1. Type and duration of opium consumption

Type of use opium	Gender	Frequency, No. (%)	*p*-value
Oral	Male (34)	18 (51)	< 0.027
	Female (25)	11 (44)	
Inhalation	Male (34)	16 (46)	< 0.040
	Female (25)	14 (56)	

Data are expressed as number (%).
χ^2 was used for statistical comparisons.

Table 2. Demographic information and clinical characteristics of the study participants in opium user and non-user patients

Variables	Opium non-user (n = 251)	Opium user (n = 60)	*p*-value
Age	48 [37–58]	58 [43–66]	0.001*
Sex			< 0.05†
Male	121 (48)	35 (58)	
Female	130 (52)	25 (42)	
DM	31 (13)	12 (20)	0.136†
HTN	48 (20)	21 (35)	0.010†
SBP	120 [110–130]	120 [120–136]	0.009*
DBP	75 [70–80]	78 [70–85]	0.783*
FBS	121 [104–145]	133 [108–184]	0.127*
BMI	28.6 ± 5.3	27.35 ± 6.05	0.103‡

Data were presented as mean ± standard deviation, median (interquartile range) or number (%).
DM, diabetes mellitus; HTN, hypertension; SBP, systolic blood pressure; DBP, diastolic blood pressure; FBS, fasting blood sugar; BMI, body mass index.
*Mann Whitney test) Q2 [Q1-Q3]; †χ^2 were used for statistical comparisons; ‡*t*-test.

https://doi.org/10.12793/tcp.2024.32.e4

Table 3. Long-term COVID-19-related diseases in opium users and non-opium users based on the disease severity

Variables	Opium non-user (n = 225)	Opium user (n = 56)	*p*-value
Non severe COVID-19			
Heart disease (positive)	6 (6)	8 (23)	0.005*
Lung disease (positive)	1 (1)	10 (29)	< 0.001*
Kidney disease (positive)	1 (1)	1 (3)	0.444*
Hospitalization days	5 [4, 5.6]	5.5 [3, 6.25]	0.978†
Overall mortality	-	-	-
Severe COVID-19			
Heart disease (positive)	7 (6)	0	0.594*
Lung disease (positive)	0	4 (19)	< 0.001*
Kidney disease (positive)	2 (1.7)	0	> 0.999*
Hospitalization days	5 [4, 7]	6 [5, 7]	0.114†
Overall mortality	0	1 (5)	0.148*

Data are presented as number (%) or median (interquartile range).
COVID-19, coronavirus disease 2019.
*χ^2 and †Mann Whitney test Q2 [Q1–Q3] were used for statistical comparisons.

The primary objective of this study was to explore the association between opium user and disease severity in hospitalized COVID-19 patients. According to our findings, in the non-severe COVID-19 group, there was a significant difference in the frequency of heart and lung diseases between opium users and non-users ($p < 0.005$ and $p < 0.001$, respectively). In contrast, in the severe COVID-19 group, only lung diseases exhibited a significant difference ($p < 0.001$). It's noteworthy that a majority of individuals with lung diseases were identified as drug users. Although opium users showed higher frequencies of hospitalization days and overall mortality compared to non-opium users, these differences did not observe statistical significance ($p > 0.05$), as detailed in **Table 3**.

Further analysis within the non-severe COVID-19 group revealed that opium users exhibited significantly lower symptoms of chills compared to non-opium users ($p < 0.05$). Overall, across both severe and non-severe COVID-19 groups, clinical symptoms were more prevalent in non-opium users than in opium users, but these variations were not statistically significant ($p > 0.05$), as presented in **Table 4**.

In the laboratory tests, the percent of lymphocyte was significantly lower in the opium positive group compared to opium negative patients ($p < 0.05$). Although, the total white blood cells (WBCs) count, the percent of neutrophil and eosinophil were higher in the opium positive group compared to opium negative patients, but these changes were not significantly. The levels of urea also were significantly higher in opium user patients compared to non-opium user patients ($p < 0.05$), **Table 5**. The initial therapies of both opium positive and negative infected patients showed not any significant changes, **Table 6**.

DISCUSSION

Following the coronavirus pandemic (COVID-19), research on the impact of smoking and drug or other substance user on the outcome of coronavirus infection has been an area of interest for the researchers through the world. The current study the relationship between opium uses and severity of disease on hospitalized COVID-19 patients in South Khorasan, Iran was investigated. Opium user is a common habit and health problem in many Middle East countries. There are beliefs about protective effects of opium consumption on several diseases including; cardiovascular disease, diabetes and respiratory disease in some

https://doi.org/10.12793/tcp.2024.32.e4

Table 4. Symptoms and signs of the study participants: a comparison between opium users and non-users based on the disease severity

Variables	Opium non-user (n = 225)	Opium user (n = 56)	*p*-value
Non severe COVID-19			
Chills	27 (26)	3 (8.6)	0.033*
Fever	51 (50)	15 (43)	0.496
Dyspnea	54 (52.4)	20 (57)	0.629
Fatigue	15 (14.6)	3 (8.6)	0.562
Anorexia	34 (33)	8 (23)	0.259
Body pain	46 (44.7)	14 (40)	0.631
Diarrhea	5 (5)	2 (5.7)	> 0.999
Sore through	7 (6.8)	3 (8.6)	0.714
Chest discomfort	13 (12.6)	3 (8.6)	0.761
Headache	23 (22.3)	6 (17)	0.515
Vertigo	15 (14.6)	1 (2.9)	0.071
Anosmia or hyposmia	17 (16.5)	2 (5.7)	0.156
Severe COVID-19			
Chills	33 (28)	3 (15)	0.279
Fever	56 (48)	6 (30)	0.138
Dyspnea	72 (61.5)	15 (75)	0.248
Fatigue	4 (3.4)	-	> 0.999
Anorexia	44 (37.6)	3 (15)	0.072
Body pain	43 (37)	9 (45)	0.482
Diarrhea	8 (6.8)	2 (10)	0.640
Sore through	10 (8.5)	1 (5)	> 0.999
Chest discomfort	8 (6.8)	2 (10)	0.640
Headache	24 (20.5)	5 (25)	0.650
Vertigo	9 (7.7)	1 (5)	> 0.999
Anosmia or hyposmia	13 (11)	1 (5)	0.692

Data are presented as number (%).
COVID-19, coronavirus disease 2019.
*χ^2 test was used for statistical comparisons.

Table 5. Baseline laboratory test results in the study participants

Variables	Opium non-user (n = 251)	Opium user (n = 60)	*p*-value
Total WBC	5.8 [4–7.58]	6.45 [5.2–7.7]	0.079
Absolute lymphocyte % (cells/mm^3)	18.7 [13.85–26.35]	17 [8.2–25.8]	0.048
Absolute neutrophil % (cells/mm^3)	69.4 [47.55–79.7]	71 [50.3–85.7]	0.184
Absolute eosinophil % (cells/mm^3)	0.00 [0.00–0.4]	0.25 [0.00–0.625]	0.125
Absolute monocyte % (cells/mm^3)	4.85 [1–8.4]	3.5 [0.5–7.65]	0.223
Baso %	0.2 [0.1–0.3]	0.2 [0.1–0.3]	0.638
LDH (U/L)	589 [439–765.2]	564 [429.7–777.25]	0.719
ALT (U/L)	31 [20–51.5]	29 [18–43]	0.096
AST	41 [28–59]	39 [24–58]	0.462
Creatinine (mg/dL)	1.01 [0.89–1.15]	1.02 [0.92–1.14]	0.544
Urea (mg/dL)	32 [23–43]	37 [26.5–48.5]	0.022
C-reactive protein (mg/L)	37 [10–56]	38.5 [15–62.7]	0.524
CPK	126.5 [81–284.5]	117 [58.3–224.5]	0.279

Data were presented as Q2 [Q1–Q3].
Mann-Whitney test was used for statistical comparisons.
WBC, white blood cells; LDH, lactate dehydrogenase; ALT, aspartate alanine transferase; AST, aspartate aminotransferase; CPK, creatinin phosphokinase.

societies, while others mention that it as an exacerbating factor for diseases [24]. Currently, the effects of opium use on the severity of COVID-19 is unclear. The results of the current study like the others showed the prevalence of male gender was significantly higher in opium group [24]. The BMI also was lower in opium user group. It has been reported that BMI was lower in opium addicted compared to the control group [25]. Diet, life style, psychosocial problems, and low economy in opium addicted patients may have had negative effects on calorie intake and leading to weight reduction in these subjects.

https://doi.org/10.12793/tcp.2024.32.e4

Table 6. Initial therapies during hospitalization in patients with history of opium uses

Variables	Opium non-user (n = 251)	Opium user (n = 60)	*p*-value
Favipiravir			0.598
Yes	6 (3)	0 (0)	
No	238 (97)	56 (100)	
Interferon.b			0.793
Yes	20 (8)	4 (7)	
No	224 (92)	52 (93)	
Dexamethazone			0.669
Yes	217 (88)	50 (90)	
No	27 (12)	5 (10)	
Remdesivir			0.991
Yes	209 (85)	48 (85)	
No	35 (15)	8 (15)	
Actemra			0.745
Yes	13 (5)	2 (4)	
No	231 (95)	54 (96)	
Ivermectin			0.160
Yes	2 (1)	2 (4)	
No	242 (99)	54 (96)	

Data are expressed as number (%).
χ^2 test was used for statistical comparisons.

The characteristics of patients including; prevalence of HTN and SBP were significantly higher, while prevalence of DM, DBP and fasting blood sugar were not significantly changes in opium user compared to the non-opium infected patients. Previously showed SBP and prevalence of high SBP were significantly higher in opium user compared to the control group, while other parameters including; blood glucose, glycated hemoglobin (HbA1c), FBS, low-density lipoprotein and DBP were not statistically significant between two groups [26]. It has been reported that opium consumption enhanced some cardiovascular diseases (CVDs) risk factors such as, HbA1c, HDL-C, lipoprotein (a) (Lpa), apolipoprotein A and B, and CRP. Lpa is an independent risk factor for premature atherosclerosis which was significantly more in opium user [27].

The results of a review study obtained from a number of animal and clinical studies indicated that opium may temporarily reduce blood pressure, but it increases blood glucose and most of blood lipids. Moreover its long term use has negative impacts and thus it aggravates diabetes, HTN and dyslipidemia [28].

The results of the current study showed in the non-severe COVID-19 group, there was a significant difference in the frequency of heart and lung diseases between opium users and non-users. In the severe COVID-19 group, only lung diseases exhibited a significant difference. Prior research has illuminated complex associations between opium consumption and cardiovascular health. While opium has been suggested to reduce lipid profiles and FBS in CVD patients, it concurrently diminishes left ventricle ejection fraction (LVEF) [24]. Notably, inflammatory lung diseases and an augmented risk of lung cancer are linked to opium use, alongside an increase in free radicals through the activation of lipid peroxidation [9]. The results of a Cohort study with 566 coronary artery bypass graft (CABG) patients, showed that opium users exhibited notably lower LVEF [29]. Moreover, the results of two other studies in CAD patients undergoing CABG confirmed significantly lower LVEF and BMI in opium-addicted individuals [30,31]. The results of these studies indicated a potential association between opium consumption and heightened incidence of heart diseases. It has been reported that opium uses cause respiratory diseases including; reported bronchitis;

bronchiolitis and pulmonary fibrosis. Also, opium use was associated with an increased risk of death from any respiratory disease (adjusted hazard ratio, 2.42–4.04).

Concurring with earlier research [32], our study indicates that opium users encountered prolonged hospitalization and increased mortality rates compared to non-users. It's crucial to acknowledge that, in our study, while these trends were observed, they did not attain statistical significance. A prior study demonstrated a noteworthy association between opium consumption and mortality in hospitalized COVID-19 patients (relative risk, 1.173) [22]. Additionally, earlier investigations highlighted notable variations in cytokine levels among opium users, with lower levels of interleukin (IL)-4 and interferon gamma, and higher levels of IL-6 and transforming growth factor-beta compared to controls [33]. It is obvious that it is essential to know mortality in COVID-19 patients is linked to the cytokine storm, driven by high levels of IL-6 [34]. These insights emphasize the intricate interplay between opium use, immune response, and health outcomes, warranting further exploration for a comprehensive understanding.

In this study, baseline vital signs, including chills, were found to be lower in opium users with non-severe COVID-19, mirroring findings from a previous study [32]. However, other vital signs in opium users, when compared to non-users, did not exhibit significant changes. Opium is known to contain over 80 different alkaloids, such as morphine (a μ receptor agonist) and codeine [35]. The observed lower signs in opium users may be attributed to the analgesic effects of opium constituents, particularly morphine.

In the laboratory tests, the percent of lymphocyte was significantly lower and the level of urea was significantly higher, while the WBC count, the percent of neutrophil and eosinophil were higher in the opium positive group that these changes were not significantly. The previous studies also indicated that opium consumption significantly increased the WBC, platelet and neutrophil count [36,37]. Administration of morphine in an experimental study also significantly increased BUN, creatinine and nitric oxide levels compared to the control mice [38]. It has been reported that Rhabdomyolysis (proteins and electrolytes release from muscle tissue) and muscle necrosis were induced by lead poisoning [39]. The results of a study also revealed the presence of lead as impurities in opium [40] that may be responsible for these adverse events. The initial therapies in the current study similar to the previous study [32] show not significant changes between opium positive and negative infected patients.

The researches for effective treatments for SARS-CoV2 introduced candidates like hydroxychloroquine, lopinavir-ritonavir, Actemra, Ivermectin, remdesivir, and favipiravir. Concurrently, the pandemic intersected with a pre-existing opioid epidemic, necessitating a closer look at the impact of these treatments on individuals with opioid use disorders [41]. Notably, smokers may have lower hydroxychloroquine response rates due to induced enzyme systems and nicotine effects [42]. Lopinavir induces methadone metabolism, causing sub-therapeutic levels and opioid withdrawal symptoms [43]. Remdesivir poses hepatotoxicity risks for those with alcohol or opioid dependence [44]. Ribavirin seems safe for substance use disorder patients, but caution is needed with tramadol and tapentadol misuse alongside favipiravir [45]. These interactions can vary based on patient characteristics and dosages. Administering COVID medications in substance use disorder patients raises concerns of poor tolerability, reduced efficacy, and increased side effects, emphasizing clinician awareness and enhanced screening.

https://doi.org/10.12793/tcp.2024.32.e4

In the current study opium uses in COVID-19 infected patients was associated with the lower weight and some vital signs at admission in COVID-19 patients but it increased disease in different organs. The opium uses were also associated with the heart and lung diseases. Psychosocial problems, low economy condition and food restrictions after opium consumption may have had negative effects on infected patients. Furthermore, analgesic effect of opium constituent especially morphine and more delayed presentation to the specific physician may have had negative effects of opium uses in the patients. More studies are needed to better determine the relationship between opium consumption and severity of COVID-19 disease.

ACKNOWLEDGMENTS

We thank the research council of Birjand University of Medical Sciences.

REFERENCES

1. Dasgupta A. Analytical true positive: poppy seed products and opiate analysis. In: Dasgupta A (ed). Crit issues alcohol drugs abuse test. Amsterdam: Elsevier; 2019, 449-462.
2. Norn S, Kruse PR, Kruse E. History of opium poppy and morphine. Dan Medicinhist Arbog 2005;33:171-184. PUBMED
3. Ziaaddini H, Ziaaddini MR. The household survey of drug abuse in Kerman, Iran. J Appl Sci (Faisalabad) 2005;5:380-382. CROSSREF
4. Sadr Bafghi SM, Rafiei M, Bahadorzadeh L, Namayeh SM, Soltani MH, Motafaker M, et al. Is opium addiction a risk factor for acute myocardial infarction? Acta Med Iran 2005;43:218-222.
5. Shahouzehi B, Shokoohi M, Najafipour H. The effect of opium addiction on serum adiponectin and leptin levels in male subjects: a case control study from Kerman Coronary Artery Disease Risk Factors Study (KERCADRS). EXCLI J 2013;12:916-923. PUBMED
6. Karbakhsh M, Salehian Zandi N. Acute opiate overdose in Tehran: the forgotten role of opium. Addict Behav 2007;32:1835-1842. PUBMED | CROSSREF
7. Marmor M, Penn A, Widmer K, Levin RI, Maslansky R. Coronary artery disease and opioid use. Am J Cardiol 2004;93:1295-1297. PUBMED | CROSSREF
8. Weihrauch D, Krolikowski JG, Bienengraeber M, Kersten JR, Warltier DC, Pagel PS. Morphine enhances isoflurane-induced postconditioning against myocardial infarction: the role of phosphatidylinositol-3-kinase and opioid receptors in rabbits. Anesth Analg 2005;101:942-949. PUBMED | CROSSREF
9. Hedayati-Moghadam M, Moezi SA, Kazemi T, Sami A, Akram M, Zainab R, et al. The effects of *Papaver somniferum* (Opium poppy) on health, its controversies and consensus evidence. Toxin Rev 2022;41:1030-1043.
10. Khachfe HH, Chahrour M, Sammouri J, Salhab H, Makki BE, Fares M. An epidemiological study on COVID-19: a rapidly spreading disease. Cureus 2020;12:e7313. PUBMED | CROSSREF
11. Khosravi M. Increasing opium use in Iran in response to unsubstantiated rumors that it protects against COVID-19. Addiction 2022;117:1173-1174. PUBMED | CROSSREF
12. Zhang JJ, Dong X, Liu GH, Gao YD. Risk and protective factors for COVID-19 morbidity, severity, and mortality. Clin Rev Allergy Immunol 2023;64:90-107. PUBMED | CROSSREF
13. Goshayeshi L, Akbari Rad M, Bergquist R, Allahyari A, Hashemzadeh K, Hoseini B; MUMS Covid-19 Research Team. Demographic and clinical characteristics of severe Covid-19 infections: a cross-sectional study from Mashhad University of Medical Sciences, Iran. BMC Infect Dis 2021;21:656. PUBMED | CROSSREF
14. Ignaszewski MJ. The epidemiology of drug abuse. J Clin Pharmacol 2021;61 Suppl 2:S10-S17. PUBMED | CROSSREF
15. Mahdavi A, Aliramezany M. Addiction and Covid-19 disease: risks and misconceptions. Addict Health 2021;13:66-67. PUBMED
16. Karam GA, Reisi M, Kaseb AA, Khaksari M, Mohammadi A, Mahmoodi M. Effects of opium addiction on some serum factors in addicts with non-insulin-dependent diabetes mellitus. Addict Biol 2004;9:53-58. PUBMED | CROSSREF

17. Hasandokht T, Salari A, Pour SS, Tirani HD, Shad B, Rajabi E. Does opium have benefit for coronary artery disease? A systematic review. Res Cardiovasc Med 2018;7:51. CROSSREF
18. Haley DF, Saitz R. The opioid epidemic during the COVID-19 pandemic. JAMA 2020;324:1615-1617. PUBMED | CROSSREF
19. Ezie C, Badolato R, Rockas M, Nafiz R, Sands B, Wolkin A, et al. COVID 19 and the opioid epidemic: an analysis of clinical outcomes during COVID 19. Subst Abuse 2022;16:11782218221085590. PUBMED | CROSSREF
20. Wainwright JJ, Mikre M, Whitley P, Dawson E, Huskey A, Lukowiak A, et al. Analysis of drug test results before and after the US declaration of a national emergency concerning the COVID-19 outbreak. JAMA 2020;324:1674-1677. PUBMED | CROSSREF
21. Ochalek TA, Cumpston KL, Wills BK, Gal TS, Moeller FG. Nonfatal opioid overdoses at an urban emergency department during the COVID-19 pandemic. JAMA 2020;324:1673-1674. PUBMED | CROSSREF
22. Mirahmadizadeh A, Heiran A, Dadvar A, Moradian MJ, Sharifi MH, Sahebi R. The association of opium abuse with mortality amongst hospitalized COVID-19 patients in Iranian population. J Prev (2022) 2022;43:485-497. PUBMED | CROSSREF
23. Zhang JJ, Cao YY, Tan G, Dong X, Wang BC, Lin J, et al. Clinical, radiological, and laboratory characteristics and risk factors for severity and mortality of 289 hospitalized COVID-19 patients. Allergy 2021;76:533-550. PUBMED | CROSSREF
24. Moezi SA, Azdaki N, Kazemi T, Partovi N, Hanafi Bojd N, Mashreghi Moghaddam HR, et al. The effects of opium uses on syntax score of angiography patients with coronary artery disease (CAD). Toxin Rev 2022;41:1246-1252. CROSSREF
25. Aghadavoudi O, Eizadi-Mood N, Najarzadegan MR. Comparing cardiovascular factors in opium abusers and non-users candidate for coronary artery bypass graft surgery. Adv Biomed Res 2015;4:12. PUBMED | CROSSREF
26. Rahimi N, Gozashti MH, Najafipour H, Shokoohi M, Marefati H. Potential effect of opium consumption on controlling diabetes and some cardiovascular risk factors in diabetic patients. Addict Health 2014;6:1-6. PUBMED
27. Asgary S, Sarrafzadegan N, Naderi GA, Rozbehani R. Effect of opium addiction on new and traditional cardiovascular risk factors: do duration of addiction and route of administration matter? Lipids Health Dis 2008;7:42. PUBMED | CROSSREF
28. Najafipour H, Beik A. The impact of opium consumption on blood glucose, serum lipids and blood pressure, and related mechanisms. Front Physiol 2016;7:436. PUBMED | CROSSREF
29. Najafi M, Jahangiry L, Mortazavi SH, Jalali A, Karimi A, Bozorgi A. Outcomes and long-term survival of coronary artery surgery: the controversial role of opium as risk marker. World J Cardiol 2016;8:676-683. PUBMED | CROSSREF
30. Eizadi-Mood N, Aghadavoudi O, Najarzadegan MR, Fard MM. Prevalence of delirium in opium users after coronary artery bypass graft surgery. Int J Prev Med 2014;5:900-906. PUBMED
31. Najafi M, Sheikhvatan M, Mortazavi SH. Do preoperative pulmonary function indices predict morbidity after coronary artery bypass surgery? Ann Card Anaesth 2015;18:293-298. PUBMED | CROSSREF
32. Rahmati A, Shakeri R, Khademi H, Poutschi H, Pourshams A, Etemadi A, et al. Mortality from respiratory diseases associated with opium use: a population-based cohort study. Thorax 2017;72:1028-1034. PUBMED | CROSSREF
33. Nabati S, Asadikaram G, Arababadi MK, Shahabinejad G, Rezaeian M, Mahmoodi M, et al. The plasma levels of the cytokines in opium-addicts and the effects of opium on the cytokines secretion by their lymphocytes. Immunol Lett 2013;152:42-46. PUBMED | CROSSREF
34. Hojyo S, Uchida M, Tanaka K, Hasebe R, Tanaka Y, Murakami M, et al. How COVID-19 induces cytokine storm with high mortality. Inflamm Regen 2020;40:37. PUBMED | CROSSREF
35. Behzadi M, Joukar S, Beik A. Opioids and cardiac arrhythmia: a literature review. Med Princ Pract 2018;27:401-414. PUBMED | CROSSREF
36. Haghpanah T, Afarinesh M, Divsalar K. A review on hematological factors in opioid-dependent people (opium and heroin) after the withdrawal period. Addict Health 2010;2:9-16. PUBMED
37. Shahabinejad G, Sirati-Sabet M, Kazemi-Arababadi M, Nabati S, Asadikaram G. Effects of opium addiction and cigarette smoking on hematological parameters. Addict Health 2016;8:179-185. PUBMED
38. Jalili C, Rashidi I, Roshankhah S, Jalili F, Salahshoor MR. Protective effect of genistein on the morphine-induced kidney disorders in male mice. Electron J Gen Med 2020;17:em213.
39. Ansari B, Dorooshi G, Lalehzar SS, Taheri A, Meamar R. Rhabdomyolysis and muscle necrosis induced by lead poisoning. Adv Biomed Res 2020;9:65. PUBMED | CROSSREF

40. Navas-Acien A, Guallar E, Silbergeld EK, Rothenberg SJ. Lead exposure and cardiovascular disease--a systematic review. Environ Health Perspect 2007;115:472-482. PUBMED | CROSSREF

41. Ghosh A, Roub F, Bisaga A. Drug treatment of SARS-Cov2: Potential effects in patients with substance use disorders (SUD). J Psychosom Res 2020;135:110159. PUBMED | CROSSREF

42. Jewell ML, McCauliffe DP. Patients with cutaneous lupus erythematosus who smoke are less responsive to antimalarial treatment. J Am Acad Dermatol 2000;42:983-987. PUBMED | CROSSREF

43. McCance-Katz EF, Rainey PM, Friedland G, Jatlow P. The protease inhibitor lopinavir-ritonavir may produce opiate withdrawal in methadone-maintained patients. Clin Infect Dis 2003;37:476-482. PUBMED | CROSSREF

44. Boettler T, Newsome PN, Mondelli MU, Maticic M, Cordero E, Cornberg M, et al. Care of patients with liver disease during the COVID-19 pandemic: EASL-ESCMID position paper. JHEP Rep 2020;2:100113. PUBMED | CROSSREF

45. Zhao Y, Harmatz JS, Epstein CR, Nakagawa Y, Kurosaki C, Nakamura T, et al. Favipiravir inhibits acetaminophen sulfate formation but minimally affects systemic pharmacokinetics of acetaminophen. Br J Clin Pharmacol 2015;80:1076-1085. PUBMED | CROSSREF