Journal of Experimental and Clinical Medicine
https://dergipark.org.tr/omujecm

Research Article

J Exp Clin Med
2022; 39(1): 226-231
doi: 10.52142/omujecm.39.1.44

Do interventional pain procedures increase the risk of COVID-19?

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Received: 21.06.2021 • **Accepted/Published Online:** 26.07.2021 • **Final Version:** 01.01.2022

Abstract

This study's main aim was to evaluate the risk of COVID-19 in patients who were performed interventional pain procedures during the pandemic. The secondary aim was to evaluate if steroid injection in the procedures increases the risk of COVID-19. In this retrospective study, the records of patients who were performed interventional pain procedures (Group I) and were only examined (Group E) between the 1st of April and 30th of November 2020 were evaluated. The rate of COVID-19 infection in the first sixty days after the hospital visit was recorded. Results of patients who were injected steroids during the procedures were also evaluated. The records of 885 patients were investigated. While 485 of them were in Group I, 400 of them were in Group E. A total of 30 patients had COVID-19 in the assessment period. COVID-19 infection rates were similar between groups. Infection rates were not increased in patients who received steroids. The infection rate was significantly higher in the first 15 days after the hospital visit in both groups comparing the remaining 45 days. We conclude that neither interventional pain procedures nor single dose steroid injections increase the risk of COVID-19. However, 'coming to hospital' is a promoting factor itself. We assume that our results are also valid for all kinds of outpatient procedures. We suggest obeying the precaution recommendation guidelines of international communities during the pandemic.

Keywords: COVID-19, pain, steroid, pandemic, outbreak

1. Introduction

At the end of 2019, a new type of coronavirus has emerged in Wuhan, China, and caused an outbreak in a short while. The World Health Organization (WHO) announced the official name of the 2019 novel coronavirus as 'Corona Virus Disease-19' (COVID-19). On the 30th of January of 2020, COVID-19 was registered as the sixth Public Health Emergency of International Concern (PHEIC) by the World Health Organization (WHO), which was officially declared as a pandemic on the 11th of March, 2020 (1,2).

According to the WHO records, COVID-19 has infected more than 155 million people and killed more than 3.2 million people worldwide. The numbers continue to increase, and the actual numbers are expected to be much higher.

Major symptoms of COVID-19 are fever, cough, fatigue, dyspnea. Minor symptoms include headache, dizziness, diarrhea, nausea, vomiting (2). The most common complication of COVID-19 is Acute Respiratory Distress Syndrome (ARDS), and other life-threatening complications are pneumonia, type-I respiratory failure, septic shock, metabolic acidosis, heart failure, renal failure, and hypoxic encephalopathy (3-6)

COVID-19 can spread by droplets, human-human contact, and indirect contact (contaminated objects and airborne contagion) (7). Due to the extremely high contagious potential of COVID-19, public places such as schools, restaurants, sports centers are closed worldwide. Particularly at the beginning period of the outbreak, almost most of the countries stopped surgical operations or treatment procedures unless they are urgent or critical for life.

COVID-19 made a huge and detrimental impact on pain treatment. Besides, pain clinics decreased their patients admitting daily capacities, and patients showed hesitation to apply to the pain clinics because of the fear of getting infected by the virus. Most pain clinics took a defensive attitude. Therefore, they canceled or postponed interventional pain procedures, considered medical treatments, and used telemedicine opportunities as much as possible.

Chronic or single-dose use of corticosteroids in the COVID-19 pandemic is another issue. Corticosteroids have immunosuppressant effects and may delay the immune response to the virus. In vitro studies have suggested that corticosteroids may impair antiviral innate immune responses (8-10).

Weak pain control is linked to the opioid crisis. It is shown that chronic pain is associated with increased mortality

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rates in cancer patients, structural and functional alterations in the brain, poverty, and decreased life expectancy when controlling for other factors (11-14). Therefore, total cessation of medical or interventional pain treatment during the pandemic would also have worse consequences.

The purpose of this retrospective study was to investigate if there is an increased risk for infection in patients who were performed interventional pain procedures in the COVID-19 outbreak. Secondary goals were to examine if there is an increased risk for patients who received corticosteroids as part of their interventions and evaluate the efficacy of the control measures applied in the clinic to prevent the virus's spread.

2. Materials and Methods

This retrospective study was conducted in the pain clinic of the anesthesiology and reanimation department of Ondokuz Mayis University Faculty of Medicine, Turkey. Approval of the institutional ethical committee was taken before the study. Data were obtained from the electronic application of the Turkish Ministry of Health and the software system of the hospital. In case of unavailability of data of a patient, information was taken by a phone conversation.

Patients older than 18 years old and admitted to the pain clinic between the 1st of April and 30th of November were included in the study. Patients were divided into two groups. Group I consisted of patients who were performed interventional pain procedures during the study period, and Group E consisted of patients admitted and examined in the pain clinic during the study period, but interventional pain procedures were not applied. Patients with cancer were not included in the study due to their possible immunosuppressive health condition to protect the study's homogeneity.

To evaluate the effects of corticosteroids on the frequency of COVID-19 infection, Group I was divided into 'Subgroup CS' and 'Subgroup NCS.' Subgroup CS consisted of patients who were injected corticosteroids in the pain procedures, while Subgroup NCS consisted of patients who were not injected corticosteroids in their procedures.

For the evaluation of infection frequencies regarding the types of the interventions, interventions classified into five groups: 1- Epidural steroid injections (ESI), 2-Radiofrequency techniques (RF), 3-Peripheric nerve blocks (PNB) and trigger point injections (TPI), 4- Intraarticular injections 5- Sympathetic blocks.

Demographic features, including the age and gender of the patients, were recorded. Positivity of COVID-19 infection following 1-15, 16-30, 31-45, and 46-60 days after the intervention or examination visit was recorded for each patient. Additionally, for patients who had got COVID-19 infection, the requirement of hospitalization, the intensive care unit (ICU) requirement, and loss of life were recorded.

Statistical analysis was performed by Statistical Package for Social Sciences (SPSS) version 15.0 program. Student t-test was used for the comparison of patients' age between groups. A Chi-square test was used for the statistical analysis of gender distribution between groups. A Chi-square test was used to analyze the frequency of COVID-19 infection between groups in specific periods. P values less than 0.05 were considered significant.

3. Results

A total of 885 patients' data were included in the study. While Group I consisted of 485 patients, Group E consisted of 400 patients. Demographic features of the patients regarding the groups were presented in Table 1. The number of females in the groups was higher than males but without statistical significance ($p=0.17$ in Group I and $p=0.47$ in Group E). The ratio of female/male was similar between Group I than Group E ($p=0.47$). The mean age of patients in Group I was higher than Group E ($p<0.001$).

Table 1. Demographic features of the individuals of the study

	Group I (n=485)	Group E (n=400)
Male	200 (41.2%)	149 (37.2%)
Female	285 (58.8%)	251 (62.8%)
Age (years)	61.0 ± 14.6	56,1 ± 16.4

There was no significant difference between Group I and Group E regarding the rate of Covid-19 infection. While 17 (3.5%) of patients in Group I had the infection, 13 (3.25 %) of Group E diagnosed the COVID-19 infection in the first 60 days after the hospital visit ($p=0.86$). There was also no significant difference in infection rates in the stated periods (Table 2).

Table 2. The frequency of COVID-19 infections and p values between Group Examination (Group E) and Group Intervention (Group I)

	0-15 days	16-30 days	31-45 days	46-60 days	Total
Group E (n=400)	5 (1.2%)	4 (1 %)	2 (0.5%)	1 (0.25 %)	13 (3.2%)
Group I (n=485)	9 (1.8 %)	4 (0.8%)	2(0.4 %)	2 (0.4%)	17 (3.5%)
P value	*0.47*	*0.78*	*0.50*	*0.67*	*0.74*
Total	14 (1.6 %)	8 (0.9 %)	4 (0.4 %)	3 (0.3 %)	30 (3.4%)

The number of patients in Subgroup CS was 307 (63.2%), and in Subgroup, NCS was 178 (26.8%). There was no significant difference in COVID-19 infection frequency between Subgroup CS and Subgroup NCS in any study's assessment periods (Table 3). There was no significant difference in terms of infection rates between the intervention types (Table 4).

Table 3. The frequency of COVID-19 infection regarding the use of steroids in the pain treatment procedures

	0-15 days	16-30 days	31-45 days	46-60 days	total
Corticosteroid + (n=307)	6 (1.9%)	3 (0.9%)	0 (0%)	2 (0.6%)	11 (3.5%)
Corticosteroid – (n=178)	3 (1.6%)	1 (0.6%)	2 (1.2%)	0 (0%)	6 (3.3%)
P value	*0.83*	*0.62*	*0.06*	*0.06*	*0.72*

When we evaluate the frequency of Covid-19 infection regarding the genders, we observed a significant elevation of infection rates in the male population in the first 30 days, particularly in 0-15 days. When we handle the whole study population of 885 pain patients, while 10 (2.8%) of males had Covid-19 infection in 0-15 days period, it was 4 (0.7%) for females (p=0.01). This significance was more evident for the males of Group I. 8 (4%) of males had the infection in 0-15 days, only one female in Group I was diagnosed with Covid-19 infection in those days (p = 0.009) (Table 5).

Table 4. The frequency of COVID-19 infection regarding the types of the interventional pain procedures

	1-15 days	16-30 days	31-45 days	46-60 days	Total (1-60 days)
Epidural Steroid injections (n= 147)	2 (1.3%)	0	1 (0.7%)	1 (0.7%)	4 (2.7%)
RF Procedures (n= 172)	3 (1.7%)	1 ((0.6%)	0	0	4 (2.3%)
PNBs or TPIs (n=92)	2 (2.1%)	2 (2.1 %)	1 (1.1%)	1 (1.1%)	6 (6.5%)
Intraarticular injections (n=49)	2 (4.0%)	0	0	0	2 (4.0%)
Sympathetic blocks (n=25)	0	1 (4.0%)	0	0	1 (4.0%)
p value	*0.72*	*0.15*	*0.15*	*0.69*	*0.45*

The mean age of thirty Covid-19 positive patients was 53.8 ±14.3 years, and the mean age of patients who did not have Covid-19 during the 60-day evaluation period was 58.7 ± 15.7 years (p=0.08).

When we discuss all the 885 patients who applied to our pain clinic in this study's evaluation period, we observed that the number of patients diagnosed with Covid-19 in a 0-15 days period was higher than all other intervals (Table 2). It was significantly higher than 31-45 days (p=0.04) and 46-60 days (0.008), but it was not significantly higher than 16-30 days (p=0.20). We observed that none of the thirty patients who had Covid-19 during the assessment period required hospitalization or advanced medical care.

4. Discussion

This study's primary aim was to search the possible inducing effect of interventional pain procedures on COVID-19 infection. The secondary aim was to search if steroid injections promote COVID-19 infection. Regarding our results, we have no evidence supporting these suspicions. However, our results were not very innocent because we detected a significant increase of the infection in the first 15 days after the hospital visit, but this finding was valid for the patients who were not performed interventional procedures. Therefore, we concluded that interventional pain procedures or single-dose steroid injections are not responsible for the infection but 'coming to hospital' is an increasing independent factor for COVID-19.

The symptoms of COVID-19 generally appear in a 7-10 days period. In their article, which was published on the 26th of March 2020, Li Q. et al. reported the incubation period to be 5.2 days; the 95th percentile of the distribution was 12.5 days (15). They also noted the mean duration from illness onset to first medical visit was 5.8 days. Nonetheless, due to the delayed incubation period or delayed medical visit, the infection diagnosis may put after 15 days in some patients. This may explain the statistically non-significant elevation in a 16-30 days period.

During the pandemic, particularly in the first months, there were no generally accepted precaution recommendations. We prepared a bundle of precautions in our clinic and strictly obeyed these items: 1- Obey on hand hygiene and general hygiene. 2- Use personal protective equipment (masks, gloves, glasses, etc.) as much as possible. 3- Reduce the number of patient admission to 50%. 4- Reduce the number of interventional procedures to 50%. 5- Consider medical treatment more than interventional treatment. 6- Avoid steroids as much as possible. 7- Use telemedicine opportunities as much as possible. 8- Change the clothing of the examination bed after each patient. 9- Limit non-essential patient escorts. 10- Do not allow more than eight patients and patient companions to exist in the clinic simultaneously. Some of our precautions were similar to the recommended guidelines of the American Medical Association (AMA), Centers for Medicare and Medicaid Services (CMS) , American Society of Regional Anesthesia and Pain Medicine (ASRA), European Society of Regional Anesthesia and Pain Therapy (ESRA), and the American Society of Pain and Neuroscience (ASPN) (16-19).

Despite the statistically significant increase of COVID-19 infection in the first 15 days after the hospital visit, we suggest that our bundle of precautions was not vain because there was no significant difference between Group E and Group I. To tell precautions were ineffective, Group I's frequency of infection in the 1-15 days period should be significantly higher due to the much longer time they pass in the pain clinic.

Table 5. The frequency of COVID-19 infection regarding the genders

Group I (n=485)					
	1-15 days	**16-30 days**	**31-45 days**	**46-60 days**	**Total**
Females (n=285)	1 (0.3%)	2 (0.7%)	2(0.7%)	2(0.7%)	7 (2.4%)
Males (n=200)	8 (4%)	2 (1%)	0	0	10 (5%)
P value	**0.009**	*0.72*	*0.68*	*0.68*	*0.13*
Group E (n=400)					
	1-15 days	**16-30 days**	**31-45 days**	**46-60 days**	**Total**
Females (n=251)	3 (1.2%)	3 (1.2%)	2 (0.8%)	1 (0.4%)	9 (3.6%)
Males (n=149)	2 (1.3%)	1 (0.7%)	1 (0.7)	0	4 (2.7%)
P value	*0.89*	*0.80*	*0.88*	*0.76*	*0.62*
Total (n=885)					
	1-15 days	**16-30 days**	**31-45 days**	**46-60 days**	**Total**
Females (n=536)	4 (0.7%)	5 (0.9%)	4 (0.7%)	3 (0.5%)	16 (3.0%)
Males (n=349)	10 (2.8%)	3 (0.9%)	1 (0.3%)	0	14 (4.0%)
P value	**0.01**	*0.91*	*0.37*	*0.45*	*0.32*

Regarding our results, the rate of COVID-19 infection of patients who received a steroid injection and patients who did not receive steroids were similar. Therefore, we could not report a correlation between steroid injection and COVID-19. Nevertheless, we do not recommend reckless use of corticosteroids in pain medicine because corticosteroids have immunosuppressant effects. Although some authors recommend treating severe COVID-19 infection, their role in promoting the infection is yet unclear (8,20,21). We declare, as an unwritten principle of our pain clinic, only equal or less than one ampule of Kenacort-A® (40 milligrams of triamcinolone acetate) or Celestone Chronodose® (6 milligrams of betamethasone) are used in our interventional procedures.

Additionally, independent from the outbreak, if a second steroid injection is necessary for the pain treatment, we wait at least four weeks between two injections. The risk of infection with steroid administration is dose-dependent, and increasing the steroid dose or shortening the interval between two steroid doses may have the potential of immunosuppression and, therefore, COVID-19 infection (22). In a multicenter study, Brenner et al. find that systemic corticosteroid use is associated with adverse COVID-19 outcomes in patients with irritable bowel syndrome (IBS) (23). Experts recommend that people taking cortisone or other steroids for chronic diseases should not stop them, except for their doctor's advice (21).

The Pain Management Community has made recommendations on using steroids for chronic pain during the COVID-19 pandemic. One Group recommends using epidural and other steroid injections at the lowest effective dose during the COVID-19 pandemic. However, the risks and benefits should still be weighed for each patient, and another group also suggests discussing treatment options with an infectious disease specialist (11,19).

According to our knowledge, this study is the first study that evaluates the frequency of COVID-19 infection following the pain treatment procedures. There are tens of different types of pain treatment interventions. We classified the procedures of our clinic into five categories to prevent mathematical chaos, and we did not observe a significant difference in COVID-19 infection rates in terms of the types of interventions.

A large-scale study demonstrated that older age and specific clinical conditions (diabetes, respiratory diseases, heart, kidney, and autoimmune conditions) are risk factors for death from COVID-19 (24). Luckily, all the thirty patients who had COVID-19 infection in the assessment period experienced the illness with mild symptoms. None of them required hospitalization or intensive care.

There are some limitations to this study. Due to the retrospective design, we could not prepare an information form including details (e. g. co-existing diseases, socio-economic status, COVID-19 history of acquaintances). Our control group did not consist of a normal population. This was due to the lack of availability to people who have no previous registration in our clinic. Another limitation was the lack of determination of asymptomatic cases. The actual ratio of asymptomatic COVID-19 cases is not known. Studies report a 1.95% to 87.9% proportion of asymptomatic individuals among all confirmed cases. Result widely differ according to the study design and the population (25-27). Another foggy area is the people who had got the disease but never applied to a health institution; therefore stayed out of records. We considered the ‘zero days’ of Group E as the patients visited the clinic and been examined. The ‘zero days’ of Group I was regarded as the day that interventional procedures were applied. However, some of these patients were admitted and been examined in the clinic a few days before the intervention day. This could cause a bias, but results did not reveal a significant COVID-19 infection increase in Group I. Therefore, we had no evidence supporting bias.

In conclusion, regarding our results, neither interventional pain procedures nor steroid injections promote the COVID-19 infection alone. However, ‘leaving home’ and ‘coming to hospital’ are risk factors for getting infected by the COVID-19 virus. Despite the lack of original studies on this issue, we assume that this study's results are also valid for all kinds of outpatient procedures (endoscopy, biopsies, magnetic resonance imaging, etc.) This outbreak continues for more than one year, and it is unclear how long it will continue more. Therefore, stopping the pain treatment facilities is not the solution. We suggest precaution recommendations of international communities are particularly useful, and each clinic should follow and implement these precautions as much as possible.

Conflict of interest

The authors have no conflict of interest to declare. The authors alone are responsible for the content and writing of the paper. None of the authors are funded by any institution or company.

Acknowledgments

COVID-19 pandemic made detrimental effects on pain treatment as well as all fields of health care. This study is about the risk of getting COVID-19 infection due to the interventional pain treatments, particularly in the treatments containing corticosteroid injections. We suggest interventional pain treatments or single or lesser dose of corticosteroid injections do not increase the risk of COVID-19 but ‘coming to hospital’ is an independent risk factor.

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