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Original Scientific Paper

THE EFFECT OF COVID-19 VACCINES ON PNEUMOTHORAX IN GERIATRIC PATIENTS HOSPİTALIZED IN INTENSIVE CARE UNIT DUE TO COVID-19

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SUMMARY – In our study, we examined the effect of COVID-19 vaccination on the incidence of pneumothorax in intensive care patients over age 65. COVID-19 intensive care patients that presented to our department between April 2020 and May 2021 during the COVID-19 pandemic were evaluated retrospectively. Patients were divided into two main groups, i.e., before and after the vaccination period. Patients were evaluated retrospectively for the following parameters: gender, age, side of pneumothorax, mortality, discharge, comorbidity, and additional pleural complications. The total number of patients was 87, i.e., 66 patients before vaccination and 21 patients after vaccination. When patients in the pre- and post-vaccination period were compared, there was a significant difference in the incidence of pneumothorax between the two groups ($p<0.05$). Pneumothorax was less common after vaccination. When patients with pneumothorax and tube thoracostomy were evaluated according to pre- and post-vaccination mortality, mortality was significantly higher (89%) in the pre-vaccination period ($p<0.05$). We consider that COVID-19 vaccines used in patients aged over 65 reduced the incidence of pleural complications, especially pneumothorax. We think that mortality due to pneumothorax in patients over 65 years of age was lower during the vaccination period. In addition, we think that bilateral pneumothorax was more common in the non-vaccinated period. As a result, we think that life-threatening pneumothorax and similar complications could be reduced by increasing the number of vaccines made in the COVID-19 pandemic and spreading it around the world.

Key words: *COVID-19; Pneumothorax; COVID-19 vaccination; Geriatrics; Intensive Care Unit; Mortality*

Introduction

Invasive mechanical ventilation may cause lung injury due to pulmonary barotrauma[1]. Pulmonary barotrauma causes air leaks into the extra-alveolar tissue, causing subcutaneous emphysema, pneumothorax, pneumomediastinum, pneumopericardium, and pneumoperitoneum[2,3]. Pulmonary barotrauma from mechanical ventilation usually occurs at high ventilation pressures (peak inspiratory pressures, plateau pressure, and positive end-expiratory pressure (PEEP)). A high PEEP is essential to prevent atelectasis and maintain lung expansion[4]. Studies have shown that patients with underlying chronic lung diseases that require invasive mechanical ventilation, such as interstitial lung

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disease, emphysema, and asthma, are more likely to develop barotrauma[5,6]. Acute respiratory distress syndrome (ARDS) has been identified as both a primary indication for mechanical ventilation and an independent risk factor for barotrauma as a complication during ventilation[5-7]. Patients with ARDS, even without mechanical ventilation, are at risk of self-induced lung injury from an increased dead space/tidal volume ratio during spontaneous breathing[8].

To date, more than 200 million cases and 4 million deaths have been recorded during the COVID-19 infection pandemic worldwide[9,10]. The COVID-19 virus is called SARS-CoV-2, and the spectrum of symptomatic SARS-CoV-2 infection ranges from mild to critical. Approximately 85% of patients have mild pneumonia and 15% are severely ill, requiring hospitalization[10-12]. An estimated 15%-70% of patients with severe disease will require mechanical ventilation due to severe hypoxemia and ARDS[13,14].

Because of the new version of SARS-CoV-2, the clinical course, factors affecting progression to ARDS, predictors of outcomes, and complications from both disease and treatment are not fully understood. Clinicians continue to rely on ongoing scientific research, anecdotal evidence, and case reports to guide patient care and management. COVID-19 has high morbidity and mortality, especially in people over age 65. It causes diffuse lung involvement and parenchymal damage[5]. In our study, we examined the effect of COVID-19 vaccination on the incidence of pneumothorax in intensive care patients over age 65.

Patients and Methods

Approval for the study was obtained from the local Ethics Committee. COVID-19 intensive care patients who presented to our department between April 2020 and May 2021 during the COVID-19 pandemic were retrospectively evaluated. The study included 87 patients referred to our department due to pneumothorax. The aim of the study was to assess the effects of COVID-19 vaccines on pneumothorax formation and prognosis in geriatric patients. Since inactive COVID-19 vaccines were administered in our country during the study, this vaccine was used in vaccinated patients. Patients were divided into two main groups, i.e., before and after vaccination. Patients were evaluated retrospectively in terms of gender, age, side of pneumothorax, mortality, discharge, comorbidity, and additional pleural complications. Patients were clinically divided into two groups as mild and severe. Nasal/mask oxygen, noninvasive ventilation and invasive mechanical ventilation were applied to patients as respiratory support. Follow-up or tube thoracostomy methods were applied to patients who developed pneumothorax. Direct radiographs were used primarily in the follow-up. If necessary, chest tomography was also used in the follow-up of some patients. Service patients who developed pneumothorax and patients lacking some information were not included in the study.

Statistical analysis

Continuous variables with normal distribution were defined using means and compared between the groups using T-test. Continuous variables with skewed distributions were defined using medians and compared between the groups using Mann-Whitney U test. The χ^2-test was used for categorical variables. Statistical analysis was performed using IBM SPSS version 20.0 (SPSS Inc., Chicago, IL, USA).

Results

Ankara City Hospital is the largest hospital in Europe with a total bed capacity of 3700, 3000 of which are on the wards and 700 in the intensive care unit. During the pandemic period, the total number of beds was increased to 5500. Due to the number of beds and being a pandemic hospital, it is the largest pandemic hospital in Europe. In our hospital, approximately 30,000 COVID-19 patients were hospitalized and followed up in the service and intensive care units during the study period. In our country, COVID-19 vaccination started from January 2021. Vaccination was primarily applied to health personnel and people over age 65. The number of patients over age 65 who were admitted to the intensive care unit in the 6-month period before vaccination was 884. During the 5-month vaccination period, the number of patients over age 65 who were admitted to the intensive care unit was 684. Intensive care patients over age 65 who presented to our department due to pneumothorax within a 1-year period were included in the study. The total number of patients was 87, i.e., 66 patients before vaccination and 21 patients after vaccination (Table 1). There were 27 fe-

male and 60 male patients, mean age 74.7 years. Tube thoracostomy was applied to all patients due to pneumothorax. Right pneumothorax was seen in 54, left pneumothorax in 16 and bilateral pneumothorax in 7 patients. All patients with bilateral pneumothorax were treated in the vaccination-free period. Subcutaneous emphysema was seen in 28, pneumomediastinum in 6, and pleural effusion pneumothorax in 5 patients. Fifty-nine patients treated before vaccination and 15 patients treated during the vaccination period died. When patients in the pre- and post-vaccination period were compared, there was a significant difference in the incidence of pneumothorax between the two groups ($p<0.05$) (Table 2). Pneumothorax was less common after vaccination. When patients with pneumothorax and tube thoracostomy were evaluated according to pre- and post-vaccination mortality, mortality was significantly higher (89%) in the pre-vaccination period ($p<0.05$).

Table 1. Epidemiological characteristics of the patient group

		Population (n)	%
Gender	Male	60	69
	Female	27	31
Mean age (years) Age range (years)	74.4 65-94		
Additional pleural complications	Subcutaneous emphysema	28	32
	Pneumomediastinum	6	7
	Pleural effusion	5	6
Side of pneumothorax	Right	54	62
	Left	26	30
	Bilateral	7	8

Table 2. Pneumothorax and mortality characteristics before and after vaccination

Pneumothorax	Non-vaccine period	Vaccine period
Population (N)	66	21
Gender (n) (male/female)	49/17	15/6
Morbidity (%)	94	81
Mortality (%)	89	70
Percentage of pneumothorax (%)	7.5	3

- When patients in the pre- and post-vaccination period were compared, there was a significant difference in the incidence of pneumothorax between the two groups. Pneumothorax was less common after vaccination ($p<0.027$).
- When patients with pneumothorax and tube thoracostomy were evaluated in terms of pre- and post-vaccination mortality, mortality and morbidity were significantly higher in the pre-vaccination period ($p<0.016$).

Discussion

The pathophysiological changes caused by dysregulation of the immune response with high inflammatory markers of COVID-19 infection may play a role in the development of pneumothorax and pneumomediastinum, independent of ventilator-induced barotrauma[15,16]. In patients who received intermittent mandatory ventilation (IMV) during development of pneumothorax, gas exchange may indicate that the more critically affected lungs are severely compromised and that the alveoli are more prone to rupture even in response to a small increase in thoracic pressure[17,18]. Several studies have noted that cystic lung changes, including bullous lung, are associated with the development of pneumothorax in hospitalized patients with COVID-19 infection[17,19-22].

The increase in the overall incidence of COVID-19-related pneumothorax from 0.3% to 12.8% in COVID-19 patients requiring IMV may be due to a more severe disease. McGuinness *et al*. report that 601 critical COVID-19 patients requiring IMV with a 57.0% mortality rate indicate a severe course of COVID-19 disease, which explains the high incidence rate of 12.8%. In addition, the incidence of pneumothorax in mechanically ventilated COVID-19 patients during this study period was higher than that in mechanically ventilated non-COVID-19 patients, indicating severe COVID-19 disease[23]. Martinelli *et al*. report that 71 hospitalized COVID-19 patients had a high incidence of pneumothorax of 84.5%. This high incidence of pneumothorax was due to the fact that 69% of the COVID-19 patients were critically ill, requiring noninvasive mechanical ventilation (NIMV), IMV, and extracorporeal membrane oxygenation (ECMO) support, and a high mortality rate of 88.3%[24]. In our study, 90 patients were followed up as intubated. Mechanical ventilation was used in pressure control mode in all patients. As low as possible PEEP values were applied. Consistent with the literature, the incidence of pneumothorax was high due to severe lung involvement of COVID-19.

Although most COVID-19 patients diagnosed with pneumothorax are male in the literature, in the study by Miro *et al*., there was no sex difference between patients diagnosed with pneumothorax and those without pneumothorax. It was observed that COVID-19-associated pneumothorax was 3.85 times more likely to occur on the right side in COVID-19 patients and was more frequent than in non-COVID-19 patients[25]. In addition, pneumomediastinum has been described more often in COVID-19 patients who were not mechanically ventilated or diagnosed with concomitant pneumothorax[24,26-30]. In our study, the number of male patients was higher, consistent with the literature. Pneumothorax of the right lung was seen in 54 patients. Unlike the literature, the most common symptom accompanying pneumothorax in our patient group was subcutaneous emphysema. Pneumomediastinum was the second accompanying symptom.

Guo *et al*. evaluated 105 elderly COVID-19 patients aged 60 to 74 years and found no difference in the incidence of pneumothorax compared to patients over 75 years of age[31]. Although chronic lung diseases such as asthma and chronic obstructive pulmonary disease (COPD) are known to be predisposing factors for the development of pneumothorax in critically ill patients, there was no correlation between pre-existing lung diseases and the risk of developing pneumothorax among COVID-19 patients, even in the absence of IMV. Miro *et al*. report that pre-existing lung diseases do not predispose COVID-19 patients diagnosed with pneumothorax and not mechanically ventilated to the development of pneumothorax[25]. In the studies by McGuinness *et al*. and Miro *et al*., there was no relationship between the development of pneumothorax in smokers with COVID-19[23,25]. In the light of the weak correlation between pre-existing lung diseases and active smoking status, pneumothorax should be considered a potential complication of hospitalized COVID-19 patients during assessment of worsening respiratory symptoms even in the absence of pulmonary comorbidities. In our study, the most common comorbid disease after hypertension was COPD. Smoking history was present in 46 patients. Similar to the literature, no significant difference was found in the effect of COPD and smoking history on the development of pneumothorax.

In the studies by McGuinness *et al*., Miro *et al*., and Ekanem *et al*., longer hospital stays were reported in COVID-19 patients diagnosed with pneumothorax compared to those without pneumothorax[22,25,32]. Additionally, according to Miro *et al*., in COVID-19 patients with pneumothorax compared to those without pneumothorax, there was a 12.9-, 4.2-, and 15.7-fold higher risk of admission to the intensive

care unit, prolonged hospitalization, and in-hospital mortality, respectively[25]. In our study, the mean length of stay in the intensive care unit was 24 days. The mortality rate was 87%. In COVID-19 patients with pneumothorax hospitalized in the intensive care unit, it was high, consistent with the literature.

In our study group, the incidence of pneumothorax was found to be significantly lower in patients over 65 years of age during the COVID-19 vaccination period. There was a significant difference between pre- and post-vaccination mortality rates in patients with pneumothorax, which were higher in the pre-vaccine period. We thought that vaccines reduced mortality by preventing complications even if patients developed COVID-19.

Limitations

Our review had a number of limitations. Real-time data such as ventilator parameters were difficult to obtain as the patients were retrospectively studied. Our study was single-center and had a limited number of patients. In addition, there were not enough studies in the literature on patients who were vaccinated due to COVID-19. For this reason, data were insufficient to be compared.

Conclusion

Pneumothorax related to COVID-19 is associated with an increased likelihood of prolonged hospitalization, intensive care unit admission, and death, particularly among elderly patients. With an increased incidence in patients requiring IMV, pneumothorax associated with COVID-19 causes a serious course of infection. We consider that COVID-19 vaccines applied to patients over 65 years of age reduce the incidence of pleural complications and especially pneumothorax. We think that mortality due to pneumothorax was lower in patients over 65 years of age during the vaccination period. In addition, we think that bilateral pneumothorax was more common in the non-vaccinated period. As a result, we think that life-threatening pneumothorax and similar complications can be reduced by increasing the number of vaccines made in the COVID-19 pandemic and spreading it around the world. Thus, it will make significant contributions to reducing the mortality of COVID-19 patients. The hypothesis needs to be supported by new multicenter studies involving a large number of patients.

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Sažetak

UČINAK CJEPIVA COVID-19 NA PNEUMOTORAKS KOD GERIJATRIJSKIH BOLESNIKA HOSPITALIZIRANIH U JEDINICI INTENZIVNOG LIJEČENJA ZBOG COVID-19

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U našem istraživanju ispitali smo učinak cijepljenja protiv COVID-19 na incidenciju pneumotoraksa kod bolesnika starijih od 65 godina hospitaliziranih u jedinici intenzivnog liječenja. Provedena je retrospektivna analiza bolesnika primljenih u jedinicu intenzivnog liječenja od travnja 2020. do svibnja 2021. godine. Bolesnici su podijeljeni u dvije glavne skupine: prije i nakon cijepljenja, a promatrani su sljedeći parametri: spol, dob, strana pneumotoraksa, smrtnost, otpust iz bolnice, supostojeće bolesti i dodatne pleuralne komplikacije. Ukupno je bilo 87 bolesnika, 66 prije cijepljenja i 21 nakon cijepljenja. Usporedba bolesnika primljenih prije i nakon razdoblja cijepljenja pokazala je značajnu razliku u incidenciji pneumotoraksa ($p<0,05$). Pneumotoraks je bio rjeđi nakon cijepljenja. Usporedba smrtnosti prije i nakon cijepljenja kod bolesnika s pneumotoraksom i torakostomijom pokazala je značajno veću smrtnost (89%) u razdoblju prije cijepljenja ($p<0,05$). Smatramo da cjepivo protiv COVID-19 kod bolesnika starijih od 65 godina snižava incidenciju pleuralnih komplikacija, osobito pneumotoraksa. Smrtnost zbog pneumotoraksa kod bolesnika starijih od 65 godina bila je niža tijekom razdoblja cijepljenja. Uz to, obostrani pneumotoraks bio je češći u vremenu prije cijepljenja. Stoga smatramo da se pneumotoraks i slične za život opasne komplikacije mogu smanjiti većom stopom cijepljenja tijekom pandemije COVID-19 širom svijeta.

Ključne riječi: *COVID-19; Pneumotoraks; Cjepivo COVID-19; Gerijatrija; Jedinica intenzivnog liječenja; Smrtnost*