DÜSTAD Dünya Sağlık ve Tabiat Bilimleri Dergisi

JOGHENS Journal of Global Health & Natural Science

ISSN: 2687-637X

Yıl: 2022 Cilt: 5 Sayı: 1

DÜSTAD
Dünya Sağlık ve Tabiat Bilimleri Dergisi

JOGHENS
Journal of Global Health & Natural Science

ISSN: 2687-637X Yıl: 2022 Cilt: 5 Sayı: 1

ULUSLARARASI EDİTÖRLER KURULU

Adı	**Ülke**
Muzaffer ALKAN	Türkiye
Ebru KAFKAS	Türkiye
İnci KESİLMİŞ	Türkiye
Kakajan Janbekov	Türkmenistan
Rahimmammet KÜRENOV	Türkmenistan
Galib SAYILOV	Azerbaycan
Seyfeddin RZASOY	Azerbaycan
Zümrüd MANSİMOVA	Azerbaycan
Eldar HACIYEV NABİYEVİÇ	Dağıstan
Ali TOPÇUK	Almanya
Necat KEVSEROĞLU	Irak
Hüseyin BEYOĞLU	Irak
Bekezhan A. AKHAN	Kazakistan
Muhtar MIROV	Kazakistan
Roza Zh. KURMANKULOVA	Kazakistan
Anara A. KARAGULOVA	Kazakistan
Eshiev ASYLBEK	Kırgızistan
Selim BEZERAJ	Kosova
Moslem SARBAST	Macaristan
Abdulqodir TOSHQULOV	Özbekistan
Obidjon SOFİYEV	Özbekistan
Svetlana Petrovna ANZOROVA	Rusya
Redzeb Skrijelj	Sibirya
Radık GALİULLİN	Tataristan
Mehmet KARATAŞ	Türkiye

MAKALELER

DÜSTAD
Dünya Sağlık ve Tabiat Bilimleri Dergisi
JOGHENS
Journal of Global Health & Natural Science
ISSN: 2687-637X Yıl: 2022 Cilt: 5 Sayı: 1

Diagnostic Values of Nitric Oxide and Hydrogen Peroxide Content in Inspired Air in Patients with Pneumonia Under Respiratory Device

Amine AKTAR KARAKAYA[1]
Yusuf TÜRKÖZ[2]
Ünsal ÖZGEN[3]

Abstract: Free radicals, especially nitric oxide (NO), are of increasing importance in the management of lung diseases. In this study, we aimed to measure the inflammatory parameters with a method that is easy to sample and does not carry any risk to the patient**.** 37 cases connected to ventilators were included (27 patients, 10 controls). On the first day and the third day, expiratory air was removed with an exhaled breath condenser, and NO, hydrogen peroxide (H_2O_2), and serum C-reactive protein (CRP) were examined. First day; The NO level of the pneumonia group was statistically higher than the control group ($p<0.0001$). No significant difference was found between the patients in terms of hydrogen peroxide levels on the first day ($p>0.05$). The decrease in NO level between the first and third days of the pneumonia group was found to be statistically significant ($p<0.05$). Serum CRP and exhaled air NO levels were significantly higher in the pneumonia group on the first day compared to the control group, but no difference was found between the H_2O_2 values. In our study, it is thought that NO is very significant in showing inflammation and may be valuable in early diagnosis, especially in respiratory device-associated pneumonia.

Keywords: exhaled air, H_2O_2, mechanical ventilation, nitric oxide, pneumonia

Solunum Cihazına Bağlı Pnömonili Hastalarda Soluk Havasındaki Nitrik Oksit ve Hidrojen Peroksitin Tanısal Değerleri

Özet: Serbest radikallerin özellikle nitrik oksitin (NO), akciğer hastalıklarının takibinde önemi giderek artmaktadır. Çalışmada, hasta için herhangi bir risk taşımayan, örneklemesi kolay bir yöntemle, enflamatuvar parametrelerin ölçülmesi planlandı. Solunum cihazına bağlı 37 olgu alındı (27 hasta, 10 kontrol). Olguların birinci ve üçüncü günlerde soluk hava yoğunlaştırıcısı ile ekspiryum hava numunesi alınarak, NO, hidrojen peroksit (H_2O_2) ayrıca serumdan C-reaktif protein (CRP) düzeyleri ölçüldü. Birinci gün; pnömoni grubunun NO düzeyi kontrol grubundan istatistiksel olarak daha yüksekti ($p<0,0001$). Birinci gün H_2O_2 düzeyi açısından gruplar arasında anlamlı bir farklılık yoktu ($p>0,05$). Pnömoni grubunun birinci ve üçüncü gün arasındaki NO düzeyindeki düşüş istatistiksel olarak anlamlı bulundu ($p<0,05$). Birinci gün bakılan serum CRP ve ekspiryum hava NO düzeyleri pnömoni grubunda anlamlı derecede yüksekti, ancak H_2O_2 düzeyleri arasında fark bulunmadı. Yapılan çalışmada, enflamasyonu göstermede NO ölçümünün oldukça anlamlı olduğu, özellikle solunum cihazına bağlı pnömonide erken tanıda değerli olabileceği düşünülmektedir.

Anahtar kelimeler: soluk havası, H_2O_2, solunum cihazı, nitrik oksit, pnömoni

[1] Corresponding author, Department of Pediatric Endocrinology, Mardin Education and Research Hospital, Mardin, Turkey, aktarkarakaya@gmail.com, 0000-0001-7004-6803
[2] Department of Medical Biochemistry, Faculty of Medicine, Inonu University, Malatya, Turkey, yusuf.turkoz@inonu.edu.tr, 0000-0001-5401-0720
[3] Department of Pediatric Hematology, Faculty of Medicine, Ondokuz Mayıs University, Samsun, Turkey, unsal.ozgen@omu.edu.tr, 0000-0002-4896-7435

INTRODUCTION

Ventilator-associated pneumonia (VAP) is an important cause of mortality and morbidity in the pediatric intensive care units and is reported to affect approximately one-tenth of children in mechanical ventilation (Chang and Schibler, 2016). In the literature, the mortality rate from VAP was found to be 13% (Kalil et al., 2016). Ventilator-associated pneumonia is defined as pneumonia that occurs 48 hours after intubation (Türk toraks derneği, 2018). New infiltrations on chest X-ray, fever and change in secretions, and increase in respiratory support requirement should warn the clinicians about VAP. Pneumonia occurring during the first four days of mechanical ventilation was called early-onset VAP, and pneumonia developed after day 4 was called late-onset VAP (Xu et al., 2019). The importance of nitric oxide (NO) is increasing in terms of early identification of patients with pneumonia under the respiratory device. Free oxygen radicals (FOR) and NO, in particular, play an important role in the development of lung diseases as well as other organs. However, the detection of these markers in the blood is not very reliable. Therefore, in patients with inflammation, to monitor the degree of the inflammatory reaction, the exhaled breath is condensed and examined. This method is preferred because of its easy applicability in evaluating the response to treatment, in the differential diagnosis, and in assessing the severity of lung diseases (Lee and Thomas 2009). It is hoped that identifying metabolites in the exhaled breath will be useful in understanding the pathophysiology of lung diseases and in the diagnosis (Bjermer et al., 2014). Increased lung stress and increased reactive oxygen radicals and NO in lung diseases have been shown in many studies (Balint et al., 2001; Kelekçi et al., 2013; Karsten et al., 2014).

To date, many studies have been conducted by collecting samples by direct inhalation of patients with asthma (Ricciardolo et al., 2015), cystic fibrosis (Balint et al., 2001), chronic obliterative bronchitis (Brugière et al., 2005) to exhaled breath condenser. In the routine follow-up of patients, the use of NO (Balint et al., 2001; Dweik et al., 2001), and hydrogen peroxide (H_2O_2) (Teng et al., 2011) parameters is recommended. Although the availability of the breath air condensation method has been shown in patients with the respiratory device (Cheah et al., 2003), as far as we can review the literature, there are only few studies on the measurement of inflammatory parameters in children with mechanical ventilator needs.

In this study, we aimed to measure the inflammatory parameters by using the EBC method which is easy to sample and does not carry any risk to the patient. In this way, we aim to demonstrate the usefulness of NO and H_2O_2 detected in exhaled breath of patients, especially in the early diagnosis of ventilator-associated pneumonia.

MATERIALS and METHODS

This study was conducted in Inönü University Faculty of Medicine, on patients under respiratory device support in pediatric and neonatal intensive care units. The patient group was composed of a total of 27 patients (19 males and 8 females) hospitalized in intensive care units, aged between one day and 10 years. As a control group, a total of 10 patients (8 boys, 2 girls) whose ages ranged from one day to 10 years without infection were evaluated. In the pneumonia group; the day on which pneumonia was diagnosed and in the control group; the day of adherence to the respiratory device was accepted as the first day. Samples were taken on the first day and the third day NO and H_2O_2 in the exhaled breath taken by the EBC method and CRP in serum were studied in the patients who were included in the study. The informed approval was taken from the parents. In this study, the approval of the ethics committee was obtained.

Clinical Pulmonary Infection Score

This scoring system is performed based on the body temperature, white blood cell count, characteristics and amount of tracheal secretions, oxygenation, chest X-ray, and tracheal aspirate culture of the patients (Table 1). This scoring system was also used in later studies. The total score of the patients in the control group was calculated as 1 point.

Table 1. Clinical pulmonary infection score (Türk Toraks Derneği, 2018).

Parameters	0 point	1 point	3 points
Body temperature (^{0}C)	≥36.1 - ≤38.4	≥38.5- ≤38.9	≥39, ≤36
White blood cell count	≥4000-≤11000	<4000, >11000	
Tracheal secretion	Absent	Non-purulent	Purulent
Oxygenization (PaO_2/FiO_2)	>240 or ARDS		<240 and no ARDS
Chest radiograph	No infiltration	Diffuse /patch infiltration	Localised infiltration
Microbiology	Insignificant microbial growth	Significant microbial growth	

ARDS: Acute respiratory distress syndrome, PaO_2: Partial arterial oxygen pressure, FiO_2: Fraction of inspired oxygen

This scoring was especially performed with the aim of early diagnosis and effective treatment of VAP, and it was stated that antibiotic use would be appropriate and effective in this way (Zilberberg and Shorr, 2010). According to the VAP report published by the American Chest Association, the diagnostic criteria for VAP are;

1-Fever

2-Infiltration in chest x-ray

3-Increased number of fragmented cells in the blood

4-Inflammatory character in tracheal secretion

The above criteria were used to diagnose pneumonia in our patients (van Oort et al., 2019). Clinical pulmonary infection scoring was used as a guide for these patients.

Exhaled Breath Condenser

The exhaled breath condenser consists of a nested cold tube assembly made of polyvinyl chloride. Patients connected to the respiratory device were assessed for their vital functions before being connected to the exhaled breath condenser. The patients were connected to EBC after humidification of the lungs at 37 °C with a humidifier in the respiratory device and after 30 minutes of opening the condenser to cool. The patient's breathing hose was connected to this system and a hose coming out of it was connected to the expiration outlet of the respiratory device. The air was condensed in about 30 minutes. While the condenser is connected, to evaluate the vital functions; pulse, oxygen saturation, blood pressure, and blood gas were monitored. For optimal evaluation, no procedures such as aspiration were performed. Since there was no gas exchange during breathing, there was no risk of infection.

Taking the Samples

After connecting the EBC, samples of 2-4 ml of exhaled air concentrate taken over 30 minutes were placed in siliconized Eppendorf tubes and stored at approximately –80°C. All chemical materials were of analytical purity. The chemical materials were obtained from Sigma Aldrich (Sigma Aldrich Chemie Gmbh, Steinheim, Germany).

Nitric Oxide Analysis

Nitric oxide is an unstable molecule. It has a short half-life, rapidly converting to nitrite (NO_2) and nitrate (NO_3). For this reason, the total nitrite (NO_2) level in biological fluids is usually suggested as an indicator of NO production (Jungersten et al., 1996). So, NO levels of the breath condensate samples were measured as total nitrite after the conversion of nitrate to nitrite. The total nitrite assay procedure was partly adapted from the method described by Ozbek et al. (2000). The total nitrite assay procedure is based on spectrophotometric measurement at a wavelength of 548 nm after the conversion of nitrite to a purple-colored azo-dye with Greiss reagent.

Hydrogen Peroxide Analysis

The hydrogen peroxide assay procedure was partly adapted from the method described by Loukides et al. (1998). The hydrogen peroxide assay procedure is based on spectrophotometric measurement of the oxidized-end product at a wavelength of 450 nm after the oxidation of tetramethylbenzidine by Horseradish Peroxidase (HRP) using hydrogen peroxide in the sample. The minimal detection limit of the method was approximately 0.1 μmol/L H_2O_2.

Ethical Statement

In this study, 2004/71 numbered ethics of İnönü University School of Medicine board approval was obtained. This study is İnönü University Scientific Research Projects Management Unit Supported by the 2005-12 project number. The study was conducted in design with the Declaration of Helsinki Ethical Principles. The informed consent form was signed by the families participating in the study.

Statistical Analyses

Statistical analyses were performed with the SPSS version 18.0 package program compatible with Windows. Results were given as mean ± standard deviation. Kolmogorov-Smirnov Test was used to determine the normal distribution of the variables in the groups ($p<0.05$). Mann-Whitney U test was used in the comparison of the patient group and the control group. Wilcoxon test was used to evaluate the change in the patient group over time. $p<0.05$ was considered to be statistically significant.

RESULTS

The age of the 27 pediatric patients under respiratory device support who were included in the study ranged from one day to 10 years, 70% were male and 30% were female. 80% of the control group was male and 20% was female. The mean age of the children in the patient group was 13.7±5.1 months and the control group was 17.8±4.2 months (Table 2). 44% of the patient group and 60% of the control group were in the newborn period (0-28 days). There was no significant difference in terms of age between the control and patient groups ($p>0.05$).

Table 2. The demographic data of the patient and control groups.

Parameters	Patient group	Control group
Age (month)	13.7±5.1	17.8±4.2
Gender (F/M)	8/19	2/8
Feeding (NG%)	52	60
Body temperature (^{0}C)		
36.5-38.4	19	10
38.5-38.9	4	-
36.4<veya 39>	4	-
White blood cell(10^3/mm^3)		
4-11	9	3
<4 or >11	18	7
Tracheal secretion		
No secretions	-	6
Serous secretion	14	4
Purulent secretion	13	-

F: Female; M: Male; NG: Nasogastric

Pneumonia was detected in 18 (66.6%) of the cases within the first 4 days after being connected to the respiratory device and 9 (33.3%) after the 4th day. The agent was detected in one of the patients with early-onset pneumonia and 6 of the patients with late-onset pneumonia. The most common microorganisms were *Pseudomonas auroginosa, Candida albicans,* and Staphylococcus. Staphylococcus was isolated in the patient with early-onset pneumonia. The most common microorganism was found to be *P. auroginosa* in late-onset pneumonia (57%). *Pseudomonas auroginosa* was detected especially in neurological patients with long-term respiratory support. *Candida albicans* was also detected in a patient with neurological problems due to long-term respiratory device support and in a patient with congenital heart disease (28%). In the control group, four patients (40%) were diagnosed with hypoxic-ischemic encephalopathy, two (20%) with congenital heart disease, two (20%) with intracranial hemorrhage, one (10%) with subacute sclerosing panencephalitis, and one (10%) with epilepsy. Two patients had CRP positivity. Patients who had a score of 1 point according to the clinical pulmonary infection scoring were considered as the control group. Body temperature was measured as 36.5-38.4 °C in 70.4% of the pneumonia group and 100% of the control group. 40 °C was the highest measured body temperature and was measured in 1 patient. Respiratory secretion was detected in patients with pneumonia. The purulen secretion ratio was evaluated as 48.2%. Increased airway secretion was observed as the primary symptom. There was a significant difference between serum CRP values in the statistical analysis of the pneumonia group and control group on the first day; p= 0.021, (Fig. 1).

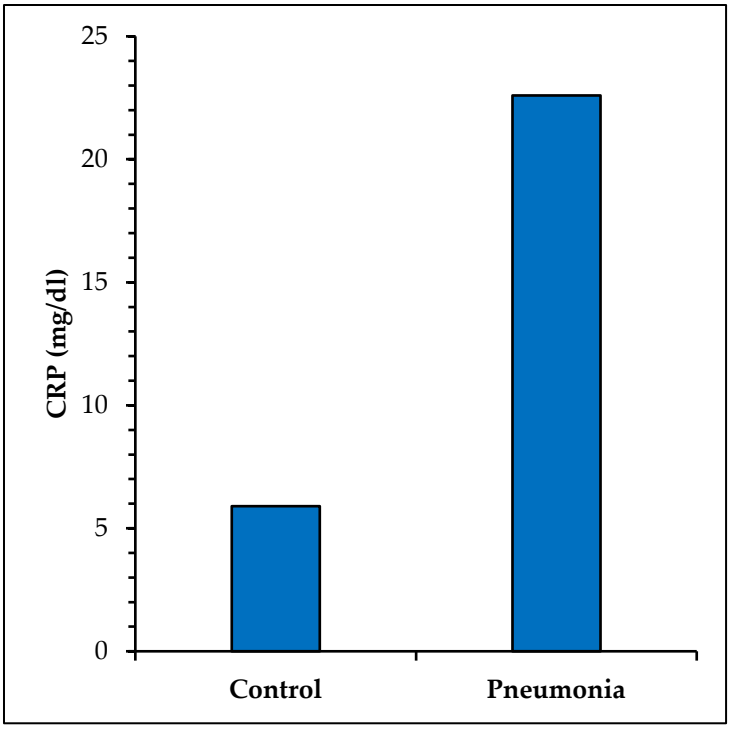


Figure1. Comparison of the first day CRP values of the pneumonia and control group.

In the statistical analysis of the pneumonia group and control group on the first day; there was a significant difference between exhaled breath NO values ($p<0.0001$) (Fig. 2).

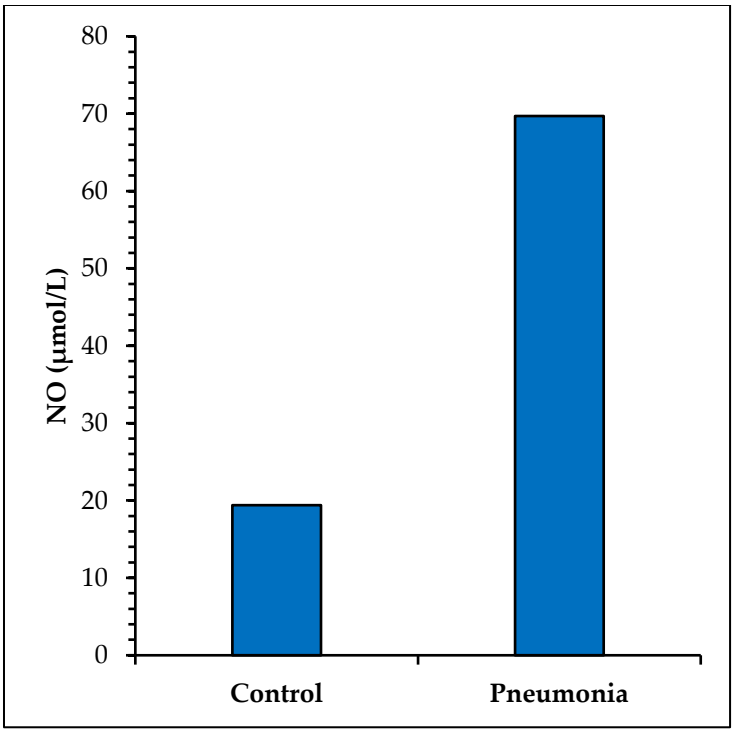


Figure 2. Comparison of the first day NO values of pneumonia and control group.

In the statistical analysis of the pneumonia group and control group on the first day; no significant difference was found in H_2O_2 analysis in exhaled breath ($p>0.05$) (Fig. 3).

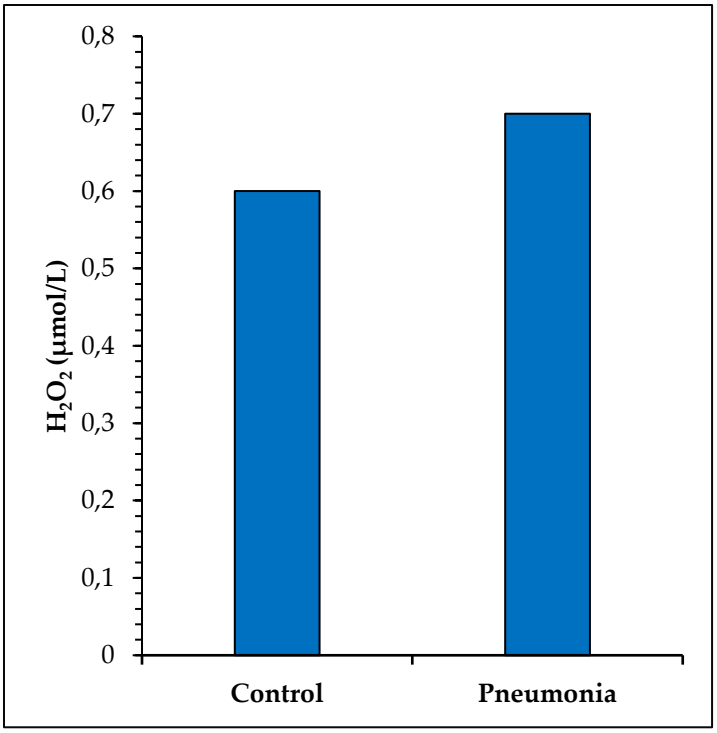


Figure 3. Comparison of H_2O_2 values of pneumonia and control group on the first day.

There was no statistically significant difference between the exhaled breath H_2O_2 values of the patients with pneumonia on the first day and the serum white blood cell count on the first day ($p>0.05$). On the first day, NO analysis was performed between the pneumonia and control groups and NO was statistically higher in the pneumonia group than the control group (69.7 ± 9.6 versus 19.4 ± 4.6) ($p<0.0001$) (Table 3). In the comparison of NO measurements on the first day and 3rd day of patients with pneumonia (69.7 ± 9.6 versus 29.5 ± 4.7), a decrease in NO during the days was statistically significant ($p<0.05$) (Table 4).

In the comparison of pneumonia and control group; there was no significant difference between them in terms of H_2O_2 values on the first day (0.7 ± 0.13 versus 0.6 ± 0.18) ($p>0.05$) (Table 3). In the comparison of H_2O_2 on the first day and 3rd day of the patients with pneumonia (0.7 ± 0.13 versus 0.2 ± 0.06), the decrease in H_2O_2 value was found to be statistically significant ($p<0.05$) (Table 4). According to the comparison of CRP levels on the first day between the pneumonia and the control group; the higher CRP value in the pneumonia group was found to be statistically significant compared to the control group (22.6 ± 6.66 versus 5.9 ± 1.77) ($p=0.021$) (Table 3). CRP values of the patients with pneumonia on the first and 3 rd day (22.6 ± 6.66 vs. 24.5 ± 7.86) were not statistically significant ($p>0.05$) (Table 4).

Table 3. The statistical comparison of the inflammatory parameters in the pneumonia and control group on the first day.

Parameters	Control	Pneumonia	*P* value
NO (µmol/L) $\bar{x}$±SD	19.4 ± 4.6	69.7 ± 9.6	0.0001
H_2O_2 (µmol/L) $\bar{x}$±SD	0.6 ± 0.18	0.7 ± 0.13	0.677
CRP (mg/dl) $\bar{x}$±SD	5.9 ± 1.77	22.6 ± 6.66	0.021

$\bar{x}$: Arithmetic mean; SD: Standard deviation

Table 4. The statistical comparison of the inflammatory parameters in the pneumonia group on the first day and 3rd.

Group	Parameters	First day	Third day	*P*
Pneumonia	NO (µmol/L) x̄±SD	69.7 ± 9.6	29.5 ± 4.7	<0.05
	H_2O_2 (µmol/L) x̄±SD	0.7 ± 0.13	0.2 ± 0.06	<0.05
	CRP (mg/dl) x̄±SD	22.6 ± 6.66	24.5±7.86	>0.05

x̄: Arithmetic mean; SD: Standard deviation

DISCUSSION and CONCLUTION

Ventilator-associated pneumonia is one of the important hospital infections that cause morbidity and mortality in patients with respiratory devices in intensive care units. There are no reliable markers to predict the onset of VAP (4). Free oxygen radicals play an important role in the development of lung diseases. The oxidant molecules cause harmful effects by disrupting the organism's structural elements, proteins, lipids, carbohydrates, nucleic acids, and necessary enzymes (Eşsizoğlu and Yıldırım, 2009; Lee and Thomas 2009). In some studies conducted so far, plasma nitrate / total nitrite ratio has been used to have an idea about NO status. Plasma nitrite and nitrate are end products of endogenous NO metabolism. In a study performed on 133 newborns, NO measurements in breath air and plasma nitrite/nitrate measurements were compared and it was concluded that NO level in breath air did not correlate with plasma nitrite/nitrate value and thus this result could not represent NO in breath air (Biban et al., 2001). Several methods have been developed over time to measure inflammation and oxidative stress of the airway. One method is induced sputum. This method is not appropriate for children and patients with severe dyspnea as it can cause bronchoconstriction and inflammatory reactions. Bronchoalveolar lavage is another method that can be used in patients, but is not preferred since it is an invasive method. Therefore, exhaled breath condensation, which is a noninvasive method, has been used to show airway inflammation and oxidative stress (Lee and Thomas 2009). EBC is used in many pulmonary diseases in both adults and children. With this method, many markers such as NO, H_2O_2, isoprostane, prostaglandins, and leukotrienes can be detected (Lee and Thomas 2009).

In our study, the NO level in the exhaled breath of children with VAP on the first day was found to be higher than the control group. Based on this data, NO was interpreted as a reliable marker in the early diagnosis of pneumonia. The fact that the NO value in the exhaled breath of the patients with pneumonia was highest on the first day and decreased on the third day was thought to be the result of suppression of inflammation in the lung due to antibiotic treatment. In a study, of 24 patients with community-acquired pneumonia who were not on a respiratory device, exhaled breath NO levels were measured before and after treatment, and it was found that NO showed a significant decrease after antibiotic treatment. In this study, it was stated that exhaled NO can be used to evaluate inflammation during pneumonia treatment and to define lung infection (Karsten et al., 2014). In another study performed on adult patients in the intensive care unit; NO, nasal NO, and plasma nitrate concentrations were measured in the exhaled breath of 49 intubated patients. In the 21 patients (43%) with pneumonia, the exhaled breath NO and nasal NO levels were found to be high when compared to the non-pneumonia group, but no difference was found between plasma nitrate levels (Adrie et al., 2001). In a study conducted on groups such as asthma, bronchiolitis obliterans, bronchiectasis, acute bacterial pneumonia, and pulmonary tuberculosis, exhaled breath NO levels of the patients were found to be significantly higher than the control group (Kelekçi et al., 2013). In all studies, no increase in NO was

shown in the case of inflammation (Carraro et al., 2008; Dikener et al., 2018). In the group of 18 community-acquired pneumonia and 17 healthy children, NO measurements were performed by examining the exhaled breath air and no significant difference could be obtained between the two groups[24]. Hydrogen peroxide can be found in expiratory air in many pulmonary diseases (ARDS, COPD, bronchiectasis, smoking) because it is an indicator of oxidative stress (Loukides et al., 1998; Ueno et al., 2008).

In our study, the statistical analysis of the first day H_2O_2 levels of pneumonia and control group was not significant ($p>0.05$), but the first day H_2O_2 values of patients with pneumonia were higher than those of 3th day ($p<0.05$). These results suggest that H_2O_2 is not a valuable enough marker in the early diagnosis of pneumonia. The fact that hydrogen peroxide was not a stable molecule was seen as a factor in the formation of this result. Similarly, in a study conducted with newborns with ventilator-dependent nasal CPAP, H_2O_2 in the exhaled breath was studied from the sample and no significant difference was found between the patient groups (Cheah et al., 2003). However, in a study on adult patients; 36 patients with a respiratory device associated with ARDS and 10 patients having respiratory device support due to extrapulmonary reasons were taken as the control group and daily hydrogen peroxide levels were compared. It was found that H_2O_2 levels increased 5 times more in the ARDS group than the control group. In the determination of hydrogen peroxide in the exhaled breath of these patients, increased levels of these oxygen radicals were associated with pulmonary infiltrative pathologies. But; it was concluded that the correlation between lung injury level and H_2O_2 level was incomplete due to the instability of this molecule and its diffusion into intact tissues (Kietzman et al., 1993).

In our study, no statistically significant correlation was found between the exhaled breath H_2O_2 values on the first day and serum white blood cell counts on the first day of the patients with pneumonia. It is assumed that the hydrogen peroxide released from the phagocytes can reach the lungs by circulation and can be detected in the exhaled breath. However, it is stated that some antioxidants in the pulmonary endothelium of pneumonia patients may prevent the passage of hydrogen peroxide from the blood to the lungs. We think that this statement may explain the correlation between hydrogen peroxide and white blood cells (Majewska et al., 2004). Our study showed that CRP values were higher in the pneumonia group compared to the control group ($p=0.021$) on the first day and CRP could be used in the early diagnosis of pneumonia. As a result; the limitation of our study was the small number of patients with pneumonia and the measurement of NO in exhaled breath and serum CRP were found to be more significant than H_2O_2 in exhaled breath. In addition, there was no statistically significant difference between exhaled breath NO and serum CRP measurements in patients with pneumonia on first day, suggesting that exhaled breath NO measurement in patients with pneumonia had no superiority to serum CRP. However, CRP is less specific than NO in pneumonia because it is not specific for lung infections and increases in the presence of infection in any part of the body. Therefore, although NO and CRP increase in pneumonia in the early period, the specificity of NO is higher and CRP is easier to perform.

In this study, it is suggested that NO measurement in exhaled breath by the EBC method can be used in the early diagnosis of pneumonia in pediatric patients with the respiratory device. Thus, it was thought that the mortality and morbidity related to VAP could be reduced and unnecessary antibiotic usage and cost could be prevented. Studies of NO in the exhaled breath in pediatric patients with respiratory devices have been reported in a small number in the literature. More comprehensive studies with a greater number of subjects are needed.

Conflict of interest: There is no conflict of interest among the authors.

REFERENCES

Adrie, C., Monchi, M., Dinh-Xuan, A. T., Dall'Ava-Santucci, J., Dhainaut, J. F., & Pinsky, M. R. (2001). Exhaled and nasal nitric oxide as a marker of pneumonia in ventilated patients. *Am J Respir Crit Care Med, 163*(5), 1143-1149.

Balint, B., Kharitonov, S. A., Hanazawa, T., Donnelly, L. E., Shah, P. L., Hodson, M. E. … Barnes, P. J. (2001). Increased nitrotyrosine in exhaled breath condensate in cystic fibrosis. *Eur Respir J, 17*(6), 1201-1207.

Biban, P., Zangardi, T., Baraldi, E., Dussini, N., Chiandetti, L., & Zachello, F. (2001). Mixed exhaled nitric oxide and plasma nitrites and nitrates in newborns infants. *Life Sciences, 68*(25), 2789-2797.

Bjermer, L., Alving, K., Diamant, Z., Magnussen, H., Pavord, I., Piacentini, G. … Usmani, O. (2014). Current evidence and future research needs for FeNO measurement in respiratory diseases. *Respir Med, 108*(6), 830-841.

Brugière, O., Thabut, G., Mal, H., Marceau, A., Dauriat, G., Marrash-Chahla, R. … Fournier, M. (2005). Exhaled NO may predict the decline in lung function in bronchiolitis obliterans syndrome. *Euro Res J, 25*(5), 813-819.

Carraro, S., Andreola, B., Alinovi, R., Corradi, M., Freo, L., Da Dalt, L. … Baraldi, E. (2008). Exhaled leukotriene B4 in children with community acquired pneumonia. *Pediatr Pulmonol, 43*(10), 982-986.

Chang, I., & Schibler, A. (2016). Ventilator associated pneumonia in children. *Paediatr Respir Rev, 20*, 10-16.

Cheah, F. C., Darlow, B. A., & Winterbourn, C. C. (2003). Problems associated with collecting breath condensate for the measurement of exhaled hydrogen peroxide from neonates on respiratory support. *Biol Neonate, 84*(4), 338-341.

Dikener, A. H., Özdemir, H., Ceylan, A., Ünlü, A., & Artaç, H. (2018). Serum periostin level and exhaled nitric oxide in children with asthma. *Asthma Allergy Immunology,16*(2), 97-103.

Dweik, R.A., Boggs, P. B., Erzurum, S. C., Irvin, C. G., Leigh, M. W., Lundberg, J. O. … Taylor, D. R. (2011). An official ATS clinical practice guideline: interpretation of exhaled nitric oxide levels (FENO) for clinical applications. *Am J Respir Crit Care Med,184*(5), 602-615.

Eşsizoğlu, A., & Yıldırım, E. A. (2009). Nitric oxide in the psychobiology of mental disorders. *Dicle Med J, 36*(1), 67-74.

Jungersten, L., Edlund, A., Petersson, A. S., Wennmalm, A. (1996). Plasma nitrate as an index of nitric oxide formation in man: analyses of kinetics and confounding factors. *Clin Physiol,16*(4), 369-379.

Kalil, A. C., Metersky, M. L., Klompas, M., Muscedere, J., Sweeney, D. A., Palmer, L. B., … Brozek, J. L. (2016). Management of adults with hospital-acquired and ventilator-associated pneumonia: 2016 Clinical Practice Guidelines by the Infectious Diseases Society of America and the American Thoracic Society. *Clin Infect Dis, 63*(5), 575-582.

Karsten, J., Krabbe, K., Heinze, H., Dalhoff, K., Meier, T., & Drömann, D. (2014). Bedside monitoring of ventilation distribution and alveolar inflammation in community-acquired pneumonia. *J Clin Monit Comput, 28*(4), 403-408.

Kelekçi, S., Sen, V., Yolbas, I., Uluca, Ü., Tan, I., & Gürkan, M. F. (2013). FeNO levels in children with asthma and other diseases of the lung. *Eur Rev Med Pharmacol Sci, 17*(22), 3078-3082.

Kietzman, D., Kahl, R., Müller, M., Burchardi, H., & Kettler, D. (1993). Hydrogen peroxide in breath condensate of patients with acute respiratory failure and with ARDS. *Intensive Care Med, 19*(2), 78-81.

Lee, W., & Thomas, P. S. (2009). Oxidative stress in COPD and its measurement through exhaled breath condensate. *Clin Transl Sci, 2*(2), 150-155.

Loukides, S., Horvath, I., Wodehouse, T., Cole, P. J., & Barnes, P. J. (1998). Elevated levels of expired breath hydrogen peroxide in bronchiectasis. *Am J Respir Crit CareMed, 158*(3), 991-994.

Majewska, E., Kasielski, M., Luczynski, R., Bartosz, G., Bialasiewicz, P., & Nowak, D. (2004). Elevated exhalation of hydrogen peroxide and thiobarbituric acid reactive substances in patients with community acquired pneumonia. *Respir Med, 98*(7), 669-676.

Ozbek, E., Turkoz, Y., Gokdeniz, R., Davarci, M., & Ozugurlu, F. (2000). Increased nitric oxide production in the spermatic vein of patients with varicocele. *Eur Urol, 37*(2), 172-175.

Ricciardolo, F. L., Sorbello, V., & Ciprandi, G. (2015). FeNO as biomarker for asthma phenotyping and management. *Allergy Asthma Proc, 36*(1), 1-8.

Teng, Y., Sun, P., Zhang, J., Yu, R., Bai, J., Yao, X., … Barnes, P. J. (2011). Hydrogen peroxide in exhaled breath condensate in patients with asthma: a promising biomarker? *Chest, 140*(1), 108-116.

Türk Toraks Derneği (2018). Erişkinlerde hastanede gelişen pnömoni. Tanı ve tedavi uzlaşı raporu, 1-4.

Ueno, T., Kataoka, M., Hirano, A., Iio, K., Tanimoto, Y., Kanehiro, A., … Tanimoto, M. (2008). Inflammatory markers in exhaled breath condensate from patients with asthma. *Respirology, 13*(5), 654-663.

van Oort, P. M., Bos, L. D., Póvoa, P., Ramirez, P., Torres, A., Artigas, A., … Martin-Loeches, I. (2019). Soluble urokinase plasminogen activator receptor for the prediction of ventilator-associated pneumonia. *ERJ Open Res, 5*(1), 00212-2018.

Xu, Y., Lai, C., Xu, G., Meng, W., Zhang, J., Hou, H., … Pi, H. (2019). Risk factors of ventilator-associated pneumonia in elderly patients receiving mechanical ventilation. *Clin Interv Aging, 7*(14), 1027-1038.

Zilberberg, M. D., & Shorr, A. F. (2010). Ventilator-associated pneumonia: the clinical pulmonary infection score as a surrogate for diagnostics and outcome. *Clin Infect Dis, 51*(S1), 131-135.

DÜSTAD
Dünya Sağlık ve Tabiat Bilimleri Dergisi
JOGHENS
Journal of Global Health & Natural Science
ISSN: 2687-637X Yıl: 2022 Cilt: 5 Sayı: 1

Evaluation of the Efficacy of Posterior Approach Quadratus Lumborum Block for Postoperative Analgesia after Lumbar Discectomy Surgery; Retrospective Observational Study

Gökhan SERTCAKACILAR[1]
Güneş Özlem YILDIZ[2]

Abstract: Lumbar disc hernia is one of the most common diseases among intervertebral disc pathologies. Lumbar discectomy surgery is, therefore, one of the leading neurosurgery interventions. Opioids are frequently used in the postoperative pain management of these patients. However, to avoid the side effects of these drugs, current block techniques are frequently used today. Quadratus lumborum block (QLB) is one of the promising blocks in this context. This study aimed to evaluate the postoperative analgesic efficacy and safety of QLB performed under ultrasound guidance in single-level lumbar discectomy surgery. Bilateral QLB was applied, 20 patients were included in the study as the block group, and 25 patients who were not applied were included in the study as the control group. Patients were evaluated in pain scores and postoperative intravenous opioid consumption at 2-6-12-24 hours postoperatively. Pain scores were significantly lower in the QLB group in all periods ($p<0.05$). Opioid consumption at the 2nd and 6th hours after the operation was significantly lower in the block group than in the control group ($p= 0.004$ and $p= 0.011$, respectively). The results of our study showed that bilateral QLB can be used as a successful option in the management of analgesia after lumbar discectomy.

Keywords: lumbar discectomy, quadratus lumborum block, postoperative analgesia, numeric rating scale

Lomber Diskektomi Cerrahisi Sonrası Postoperatif Analjezi Amacıyla Uygulanan Posterior Yaklaşımlı Quadratus Lumborum Bloğunun Etkisinin Değerlendirilmesi; Retrospektif Gözlemsel Çalışma

Özet: Lomber disk hernileri intervertebral disk patolojileri içerisinde en sık görülen hastalıklardan birisidir. Lomber diskektomi, bu nedenle beyin cerrahisi girişimlerinin başında gelmektedir. Bu hastaların postoperatif dönemdeki ağrı

[1] Corresponding author, Department of Outcomes Research, Anesthesiology Institute, Cleveland Clinic, Cleveland, OH, USA & Department of Anesthesiology and Reanimation, University of Health Science, Bakırköy Dr. Sadi Konuk Education and Research Hospital, Istanbul, Turkey, drgokhansertcakacilar@gmail.com, 0000-0002-4574-0147.
[2] Department of Anesthesiology and Reanimation, University of Health Science, Bakırköy Dr. Sadi Konuk Education and Research Hospital, Istanbul, Turkey, drgunesim@hotmail.com, 0000-0002-4557-9517.

yönetiminde opioidler sık olarak kullanılmaktadır. Bu ilaçlara ait yan etki insidansından kaçınmak için günümüzde güncel blok teknikleri sıklıkla kullanılır olmuştur. Quadratus lumborum bloğu da (QLB) bu bağlamda gelecek vaad eden bloklardan birisidir. Bu çalışmada, tek seviye lomber diskektomi cerrahisinde ultrason eşliğinde uygulanan QLB'nun postoperatif analjezik etkinliği ve güvenliğinin değerlendirilmesi amaçlanmıştır. Bilateral QLB uygulanan 20 hasta blok grubu olarak ve uygulanmayan 25 hasta ise kontrol grubu olarak çalışmaya dahil edildi. Ameliyat sonrası 2-6-12-24. saatlerde hastaların ağrı skorları ve postoperatif iv opioid tüketimleri değerlendirildi. Ağrı skorları tüm zaman dilimlerinde QLB grubunda anlamlı şekilde düşük saptandı ($p<0.05$). Operasyon sonrası 2. ve 6. saatlerde opioid tüketimi, kontrol grubuna kıyasla blok grubunda anlamlı olarak daha düşük bulundu ($p=0.004$ ve $p=0.011$, sırasıyla). Çalışmamızın sonuçları bilateral quadratus lumborum bloğunun lomber diskektomi operasyonu sonrası analjezi yönetiminde başarılı bir seçenek olarak kullanılabileceğini göstermiştir.

Anahtar kelimeler: lomber diskektomi, quadratus lumborum bloğu, postoperatif analjezi, sayısal derecelendirme ölçeği

INTRODUCTION

Lumbar disc hernia is the most common intervertebral disc pathology and requires surgery when symptomatic (Parker et al., 2015). Lumbar disc herniation may be asymptomatic depending on the severity of the deformity, or it may cause symptoms that require an urgent operation, such as severe pain and a foot drop (Kortelainen et al., 1985). The main indications for surgical treatment are nerve compressions, weakness in the lower extremities, and low foot development (McGirt et al., 2009; Postacchini and Postacchini, 2011). Postoperative pain may prevent patient mobilization, leading to deterioration in the quality of daily life, postoperative pulmonary complications, and prolongation of hospital stay (Fjeld et al., 2019). Opioid agents are frequently preferred in the postoperative pain management of patients who have undergone lumbar discectomy (Krebs et al., 2010). However, these techniques can have many side effects such as nausea, vomiting, urinary retention, and sedation (Zhao et al., 2004). To avoid the incidence of side effects of these drugs, current block techniques are frequently used today. Erector spinae plane block (ESPB), one of the truncal blocks, has been used in many studies for pain management after lumbar discectomy surgery (Ueshima et al., 2019). In recent years, the quadratus lumborum block (QLB) defined by Blanco et al. (2015) has also been used for effective and safe postoperative analgesia after abdominal surgeries such as cholecystectomy, cesarian, and hysterectomy, and it has been reported to provide an effect (Blanco et al., 2015). Different studies have suggested that analgesia can be provided in the thoracic and lumbar areas after QLB and affects both somatic pain and visceral pain (Ishio et al., 2017; Okur et al., 2021). This study aimed to evaluate the postoperative analgesic efficacy and safety of ultrasound-guided QLB in patients who had a single-level lumbar disc herniation.

MATERIALS and METHODS

Study design

After obtaining approval from the Clinical Research Ethics Committee of the training and research hospital (2021/272), where the study will be conducted Sept 2020 – Dec 2020 dates patients between the ages of 18-70 who underwent lumbar discectomy with the microdissection technique and with physical status I-II of the American Society of Anesthesiologists (ASA) were included in the study. Patients operated on at more than one level had missing information on pain follow-up forms, had ASA ≥ 3, and patients with body mass index > 35kg/m^2 were excluded from the study (Fig. 1). Hospital computer documentation systems and patient pain follow-up forms were used to collect data. Since the study was retrospective, patient

records were reviewed retrospectively. Consecutive patients who met the inclusion criteria were analyzed in either intravenous (iv) opioid or QLB groups according to the analgesic method they received. The study was carried out following the principles set out in the Declaration of Helsinki.

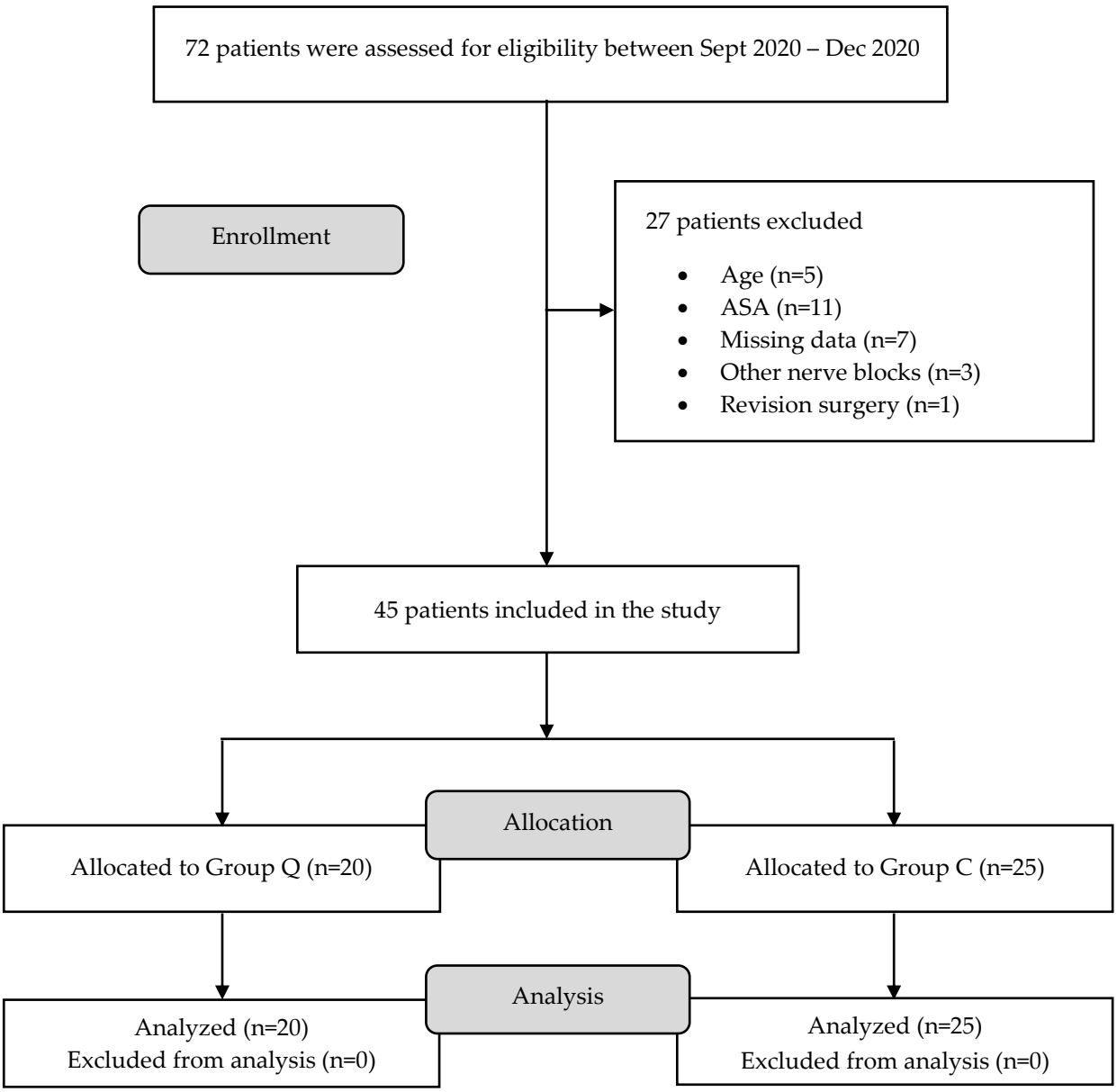


Figure 1. CONSORT flow chart of the study

General anesthesia technique

Before the operation, 22-gauge vascular access was established in all patients, and infusion was started with 2-4 mL/kg/h isotonic solution; standard monitoring was achieved with electrocardiography (ECG), noninvasive blood pressure, and peripheral oxygen saturation (SpO_2). 0.03-0.05 mg/kg midazolam was administered to all patients for premedication. After anesthesia induction was provided with 1.5 μg/kg fentanyl, 2-3 mg/kg propofol, and 0.6-0.8 mg/kg iv rocuronium, the patients were intubated. Anesthesia

was maintained with 3% desflurane in 40% oxygen in the air with a total inflow of 3 L/min and iv remifentanil infusion (0.05-0.1 μg/kg/min). All patients were administered 1 g iv paracetamol while the surgical field was closed and 4 mg ondansetron for postoperative nausea and vomiting prophylaxis. At the end of the surgery, all patients were kept in the recovery room in room air for 15 minutes. After being followed up, those with an Aldrete score ≥ 9 were sent to the service.

Quadratus lumborum block technique

Quadratus lumborum (QL) block was performed under ultrasound guidance before the surgical procedure, after the patients were placed in the prone position, following anesthesia and endotracheal intubation. A single anesthesiologist (GS) applied QL block to all patients with at least five years of experience. Block application was performed using a 100 mm 22 gauge needle (Stimuplex Ultra 360 30° - BRA-04892510-01 / B. Braun Melsungen AG, Japan) and a linear multifrequency 12L probe of the ultrasonography device (General Electric VIVID e model, GE Medical Systems, Phoenix-USA) after asepsis conditions were achieved in the operation area. While the patient was in the prone position, the QL muscle and the psoas major muscle were visualized 2-3 cm lateral to the midline at the lumbar vertebra level to be operated on, and the needle was advanced between these two muscles by entering with the in-plane technique (Fig. 2). The needle was offered up to the anterior thoracolumbar fascia between the middle layer of the thoracolumbar fascia and the posterior border of the QL muscle. After controlling the location of the needle with 2-3 ml of saline and then aspiration, 20 ml of 0.25% bupivacaine was injected into the posterior of the QL muscle. Then the same procedure was applied to the opposite side using the same dose.

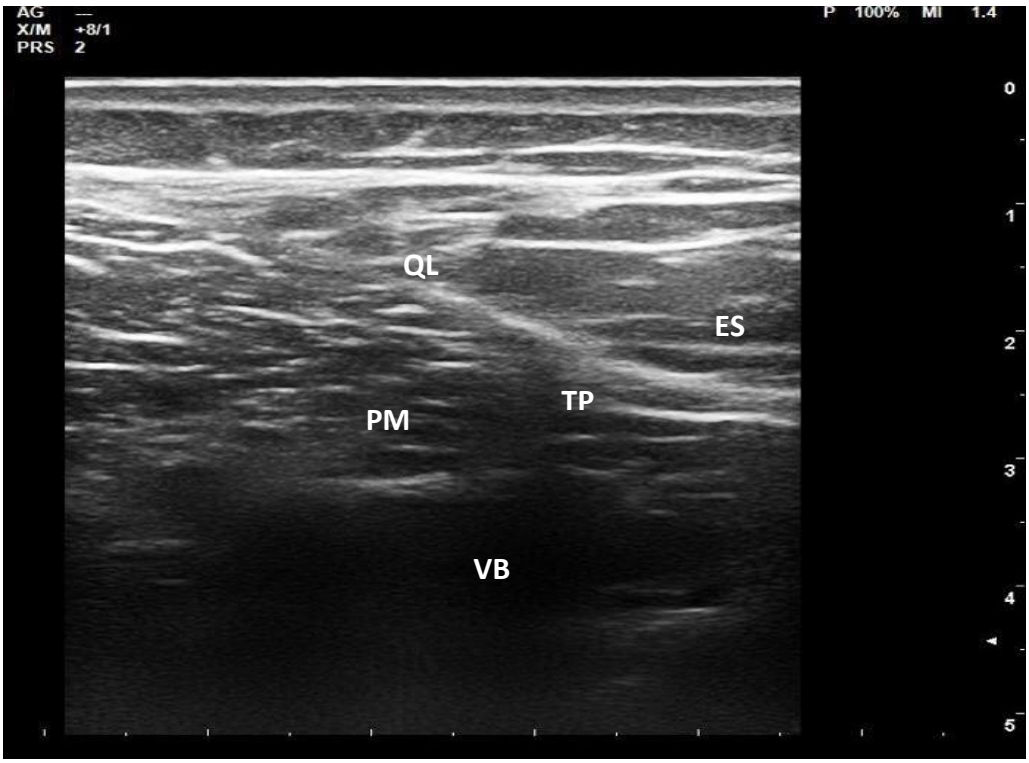


Figure 2: Sonographic anatomy of the QL block (QL: Quadratus lumborum muscle, PM: Psoas major muscle, ES: Erector spinae group of muscle, TP: Transverse process, VB: vertebral body).

Postoperative management

All patients were routinely administered 1 g of paracetamol at 12-hour intervals to provide analgesia in the postoperative period. Patients were evaluated in pain scores and analgesic needs at 2-6-12-24 hours postoperatively. Postoperative pain was assessed using a numeric rating scale (NRS, 0-10; 0 = no pain and 10 = excruciating pain). If the patients' pain scores were greater than four, 30 mg of tramadol hydrochloride was applied to a maximum of 120 mg within 24 hours. In addition, 20 mg of tenoxicam was administered as rescue analgesia in patients with a pain score of ≥ 4, as a maximum of two doses per day. Patients' total opioid and rescue analgesic doses and opioid-related complications such as nausea, vomiting, pruritus, and urinary retention were recorded in the first 24 hours.

Outcome measurements

The primary outcome measure of the study was the NRS scores in the first 24 hours postoperatively between the QLB and control groups. Secondary outcome measures were total opioid consumption and opioid-related complications.

Statistical analysis

The G*Power 3.1.9.2 program was used to calculate the sample size of the study. A pilot retrospective study was conducted with ten patients from each group to determine the minimal sample size for the primary outcome. The mean NRS value was 1.4±1.18 in Group Q and 2.95±1.54 in Group C. An α error = 0.05 with a power of 95% was assumed so that each group had at least seventeen participants. We included 20 patients in Group Q and 25 patients in Group C due to the possibility of dropouts. Patient data from the pilot study were not included in the main study.

The data collected in the study were evaluated with the SPSS 22.00 program for Windows 10. The Kolmogorov-Smirnov test was used to check the normality of the data distributions. Categorical variables are given as percentages (%) and numerical variables as mean ± standard deviation for descriptive statistics. In comparing the quantitative data of the two groups when the normality conditions are met, the Two-Sample Independent T-test was used. In contrast, Fisher's Exact Test was used when the variables were qualitative. Mann-Whitney U test was used for quantitative variable data comparisons where normality conditions were not met. The statistical significance level of alpha was accepted as $p<0.05$.

RESULTS

The files of 72 consecutive patients who underwent lumbar discectomy were reviewed retrospectively for the study. Twenty-seven patients were excluded from the study due to missing data, age, other truncal blocks, ASA, and revision surgery (Fig. 1). Demographic data and clinical features of both groups were similar (Table 1). Pain scores were significantly lower in the QLB group (Group Q) than the control group (Group C) in all periods (Table 2). When opioid consumption was compared between the groups, opioid consumption at the 2nd and 6th hours after the operation was significantly lower in the block group than the control group ($p=0.004$ and $p=0.011$, respectively) (Table 2). There was no significant difference between the two groups in the use of rescue analgesic requirements ($p=0.161$). The two groups were similar in opioid-related side effects such as nausea and vomiting ($p=0.260$ and $p=0.242$, respectively) (Table 3).

Table 1. Comparison of the demographical and clinical data between groups Q and C.

		Group Q (*n*=20) Mean ± SD/n-%	**Group C** (*n*=25) Mean ± SD/n-%	***p* value**
Age		48.70±14.31	46.72±12.86	0.628*
Gender				
	Female	10 (50%)	11 (14.03%)	0.688†
	Male	10 (50%)	14 (85.9%)	
BMI		24.47±2.56	23.63±2.76	0.305*
ASA				
	I	7 (17.6%)	9 (15.7%)	0.944†
	II	13 (77.9%)	16 (73.6%)	
Duration of surgery (min)		85.7±22.31	80.08±15.03	0.320*
Duration of anesthesia (min)		112.65±21.43	103.47±19.27	0.203*
Level of surgery (L_2-L_3 / L_3-L_4 / L_4-L_5 / L_5-S_1)		1/3/16/0	1/5/18/1	0.918†

Data are presented as mean±standard deviation (SD) or number (%).
BMI: body mass index, ASA: American Society of Anesthesiologists.
* Independent Sample t-test
† Chi-square test

Table 2. Comparison of opioid consumption and NRS scores between groups Q and C.

	Group Q (*n*=20) Mean ± SD/n	**Group C** (*n*=25) Mean ± SD/n	***p* value**
Opioid consumption			
PO 2nd h	1.50±6.70	13.20±15.19	0.004*
PO 6th h	4.50±10.99	15.60±15.29	0.011*
PO 12th h	7.5±13.32	14.40±15.29	0.118*
PO 24th h	6.0±12.31	13.20±15.19	0.093*
Rescue analgesic requirement	7/13	14/11	0.161†
NRS			
PO 2nd h	0.60±0.94	3.52±1.55	< 0.001*
PO 6th h	1.20±1.15	3.64±1.52	< 0.001*
PO 12th h	2.65±1.30	3.52±1.41	0.028*
PO 24th h	2.45±1.66	3.72±1.51	0.021*

Data are presented as mean±standard deviation (SD) or number.
NRS: numerical rating scale, PO: postoperative, h: hour
*Mann-Whitney u test, †Chi-square test (Fischer test)

Table 3. Comparison of incidence opioid related adverse effects between groups Q and C.

Opioid related complications	Group Q (n=20)	Group C (n=25)	p value
Breathing depression (Y/N)	0/20	0/20	1.000*
Sedation (Y/N)	0/20	0/20	1.000*
Nausea (Y/N)	2/18	7/18	0.260*
Vomiting (Y/N)	0/20	3/22	0.242*
Itching (Y/N)	0/20	0/20	1.000*

Data are presented as numbers. Y: Yes, N: No
*Fischer exact test

DISCUSSION and CONCLUSION

Ultrasound-guided QL block in single-level lumbar discectomy surgery provided more effective pain control and lower doses of opioid consumption compared to standard multimodal analgesic administration. The analgesic efficacy of this block has been determined in randomized controlled studies of QL block in abdominal surgeries such as cholecystectomy, inguinal hernia, sectional and colorectal procedures (Akerman et al., 2018; Gurbet et al., 2014; Postacchini and Postacchini, 2013). This retrospective cohort study is the first in the literature to investigate the efficacy of QL block in postoperative pain management in lumbar discectomy surgery.

Patients experience moderate to severe pain in the first 24 hours after lumbar discectomy (McGirt et al., 2009). Today, truncal blocks have started to be preferred over opioid analgesia due to lower complication risk and more stable hemodynamics. QLB is an "interfacial plane block" that was first described by Blanco in 2007 as an alternative to the TAP block (Blanco, 2007). In lumbar discectomy operations, iv analgesics with different action mechanisms such as paracetamol, non-steroidal anti-inflammatory drugs, and opioids have been combined. With the use of ultrasonography, truncal plane blocks, which have become more common in clinical practice and have decreased complication rates, have also become an indispensable part of multimodal analgesia protocols (Saadawi et al., 2021). QL block has also been frequently used for postoperative analgesia, especially in abdominal surgery (Kadam, 2013; Murouchi et al., 2016; Ueshima et al., 2017).

After the block was defined, two different studies have been published comparing the posterior QL block with the TAP block, reporting that the posterior approach is more effective than the lateral approach and provides less opioid consumption. The posterior QLB is a posterior abdominal wall block targeting the mid-thoracolumbar fascia (TLF). Due to the character of the fascia, dermatomal spread in the QL block may be greater due to distribution to the lumbar plexus or paravertebral region (Elsharkawy et al., 2017). In the posterior QL block, a local anesthetic is injected behind the QL muscle, more precisely between the medial lamina of the TLF and the QL muscle, which separates the QL muscle from the latissimus dorsi and paraspinal muscles. This method can produce an effective analgesic in lumbar spine surgery because the local anesthetic can spread to the transverse process and block the posterior branches of the lumbar spinal nerve.

In the studies published so far on this block, the authors agree that QLB generally produces an analgesic effect with long duration and low pain scores. In a study in which posterior QLB was applied, the spread of local anesthesia applied to the paravertebral area was suggested as a potential mechanism of action due

to the anatomical connection between the fascia transversalis and the endothoracic fascia. In this published cadaver study, however, the opposite opinion was expressed, and they stated that in previous studies, a paravertebral local anesthetic applied did not spread to the lumbar region, and the effect of QLB on visceral pain was realized through the sympathetic chain or celiac ganglion blockade (Kumar et al., 2017). In another cadaveric study, it was stated that lumbar plexus involvement is possible with posterior QLB (Carline et al., 2016).

In the present study, similar to previous studies, patients who underwent QLB for postoperative analgesia had lower pain levels and opioid consumption in the first 24 hours (Hansen et al., 2019). This is also important in early mobilization, shortening hospital stay, and reducing costs. In another study, QL block was compared with systemic analgesia in patients who underwent, supporting our results. In addition, it was reported that opioid use and pain scores were significantly lower in the block group (Ökmen et al., 2018).

In this study, postoperative opioid consumption was significantly lower in the Group Q, especially at the 2nd and 6th hours. Although opioid consumption was lower at 12 and 24 hours compared to Group C, no significant difference was found. It can be said that the reason for this is the effect of iv analgesic applied to the patients at the end of the surgery. The detection of similar opioid consumption between the two groups at the 24th hour indicates that the block's effect did not reach until the 24th hour, despite the use of long-acting local anesthetics in the study. In some studies, it has been shown that opioid use gradually increases towards the 24th hour in different types of peripheral nerve blocks performed with bupivacaine (Bramlett et al., 2012).

The findings obtained in the study showed that QL block might provide benefit as regional analgesia in patients who underwent single-level lumbar discectomy. USG guided QLB is an easy to apply and safe block in the prone position. It can be used quickly when the patient is returned to the prone position after induction. In this study, although the duration of anesthesia was longer in Group Q, no statistically significant difference was found between the two groups. Although it is stated that complications such as intravascular or retroperitoneal injection may rarely develop, performing the procedure under ultrasound will minimize the risk of complications. In the present study, similar to the literature, no procedure-related difficulties were experienced in the patients.

The study has some limitations. Since the study was in a retrospective cohort design, randomization could not be done to select patients in the study, and the patients were included in the study consecutively according to the order of admission. In addition, due to the small number of patients in the study and the fact that the study was carried out in a single center, the results may not reflect the general population. Finally, dermatomal evaluation of the patients could not be performed after the procedure since the blocks were performed after the induction of anesthesia.

The presented study showed that bilateral single shut QL block in single-level lumbar discectomy surgery can be used as a successful option in postoperative analgesia management by significantly reducing opioid consumption and pain scores. However, more studies are needed to evaluate the effectiveness of the block to include QL block in multimodal analgesia procedures in lumbar discectomy surgery.

Author contribution: All authors contributed to the study's conception and design. Conception and design, Provision of study materials, Data collection or management, Manuscript writing, Final approval: GS, Study design, Manuscript preparation, Language editing, Statistical analysis: GOY. All the authors contributed to the interpretation of the results and the proofreading of the manuscript.

Ethics approval: The trial was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Ethics Committee of the Bakirkoy Dr. Sadi Konuk Training and Research Hospital (approval number: 2021/272, approval date:03/05/2021).

Conflict of interest: There is no conflict of interest among the authors.

REFERENCES

Akerman, M., Pejčić, N., & Veličković, I. (2018). A Review of the Quadratus Lumborum Block and ERAS. *Frontiers in medicine, 5*, 44.

Blanco, R. (2007). 271: Tap block under ultrasound guidance: the description of a "no pops" technique. *Regional Anesthesia & Pain Medicine, 32*, 5, suppl; 130.

Blanco, R., Ansari, T., & Girgis, E. (2015). Quadratus lumborum block for postoperative pain after caesarean section: A randomised controlled trial. *European Journal Of Anaesthesiology, 32*(11), 812–818.

Bramlett, K., Onel, E., Viscusi, E. R., & Jones, K. (2012). A randomized, double-blind, dose-ranging study comparing wound infiltration of DepoFoam bupivacaine, an extended-release liposomal bupivacaine, to bupivacaine HCl for postsurgical analgesia in total knee arthroplasty. *The knee, 19*(5), 530–536.

Carline, L., McLeod, G. A., & Lamb, C. (2016). A cadaver study comparing spread of dye and nerve involvement after three different quadratus lumborum blocks. *British Journal of Anaesthesia, 117*(3), 387–394.

Elsharkawy, H., El-Boghdadly, K., Kolli, S., Esa, W., DeGrande, S., Soliman, L. M., & Drake, R. L. (2017). Injectate spread following anterior sub-costal and posterior approaches to the quadratus lumborum block: A comparative cadaveric study. *European Journal of Anaesthesiology, 34*(9), 587–595.

Fjeld, O. R., Grøvle, L., Helgeland, J., Småstuen, M. C., Solberg, T. K., Zwart, J. A., & Grotle, M. (2019). Complications, reoperations, readmissions, and length of hospital stay in 34 639 surgical cases of lumbar disc herniation. *The Bone & Joint Journal, 101-B*(4), 470–477.

Gurbet, A., Bekar, A., Bilgin, H., Ozdemir, N., & Kuytu, T. (2014). Preemptive wound infiltration in lumbar laminectomy for postoperative pain: comparison of bupivacaine and levobupivacaine. *Turkish Neurosurgery, 24*(1), 48–53.

Hansen, C. K., Dam, M., Steingrimsdottir, G. E., Laier, G. H., Lebech, M., Poulsen, T. D., Chan, V., Wolmarans, M., Bendtsen, T. F., & Børglum, J. (2019). Ultrasound-guided transmuscular quadratus lumborum block for elective cesarean section significantly reduces postoperative opioid

consumption and prolongs time to first opioid request: a double-blind randomized trial. Regional anesthesia and pain medicine, rapm-2019-100540. Advance online publication.

Ishio, J., Komasawa, N., Kido, H., & Minami, T. (2017). Evaluation of ultrasound-guided posterior quadratus lumborum block for postoperative analgesia after laparoscopic gynecologic surgery. *Journal of Clinical Anesthesia, 41*, 1–4.

Kadam V. R. (2013). Ultrasound-guided quadratus lumborum block as a postoperative analgesic technique for laparotomy. *Journal of Anaesthesiology, Clinical Pharmacology, 29*(4), 550–552.

Kortelainen, P., Puranen, J., Koivisto, E., & Lähde, S. (1985). Symptoms and signs of sciatica and their relation to the localization of the lumbar disc herniation. *Spine, 10*(1), 88–92.

Krebs, E. E., Lurie, J. D., Fanciullo, G., Tosteson, T. D., Blood, E. A., Carey, T. S., & Weinstein, J. N. (2010). Predictors of long-term opioid use among patients with painful lumbar spine conditions. *The Journal of Pain, 11*(1), 44–52.

Kumar, A., Sadeghi, N., Wahal, C., Gadsden, J., & Grant, S. A. (2017). Quadratus Lumborum Spares Paravertebral Space in Fresh Cadaver Injection. *Anesthesia and Analgesia, 125*(2), 708–709.

McGirt, M. J., Ambrossi, G. L., Datoo, G., Sciubba, D. M., Witham, T. F., Wolinsky, J. P., Gokaslan, Z. L., & Bydon, A. (2009). Recurrent disc herniation and long-term back pain after primary lumbar discectomy: review of outcomes reported for limited versus aggressive disc removal. *Neurosurgery, 64*(2), 338–345.

Murouchi, T., Iwasaki, S., & Yamakage, M. (2016). Quadratus Lumborum Block: Analgesic Effects and Chronological Ropivacaine Concentrations After Laparoscopic Surgery. *Regional Anesthesia and Pain Medicine, 41*(2), 146–150.

Okur, O., Karaduman, D., Tekgul, Z. T., Koroglu, N., & Yildirim, M. (2021). Posterior quadratus lumborum versus transversus abdominis plane block for inguinal hernia repair: a prospective randomized controlled study. *Brazilian Journal of Anesthesiology (Elsevier), 71*(5), 505–510.

Ökmen, K., Metin Ökmen, B., & Topal, S. (2018). Ultrasound-guided posterior quadratus lumborum block for postoperative pain after laparoscopic cholecystectomy: A randomized controlled double blind study. *Journal of Clinical Anesthesia, 49,* 112–117.

Parker, S. L., Mendenhall, S. K., Godil, S. S., Sivasubramanian, P., Cahill, K., Ziewacz, J., & McGirt, M. J. (2015). Incidence of Low Back Pain After Lumbar Discectomy for Herniated Disc and Its Effect on Patient-reported Outcomes. *Clinical Orthopaedics and Related Research, 473*(6), 1988–1999.

Postacchini, F., & Postacchini, R. (2011). Operative management of lumbar disc herniation. *Advances in Minimally Invasive Surgery and Therapy for Spine and Nerves,* 17-21

Saadawi, M., Layera, S., Aliste, J., Bravo, D., Leurcharusmee, P., & Tran, Q. (2021). Erector spinae plane block: A narrative review with systematic analysis of the evidence pertaining to clinical indications and alternative truncal blocks. Journal of clinical anesthesia, 68, 110063.

Ueshima, H., Inagaki, M., Toyone, T., & Otake, H. (2019). Efficacy of the Erector Spinae Plane Block for Lumbar Spinal Surgery: A Retrospective Study. *Asian Spine Journal, 13*(2), 254–257.

Ueshima, H., Otake, H., & Lin, J. A. (2017). Ultrasound-Guided Quadratus Lumborum Block: An Updated Review of Anatomy and Techniques. *Biomed Research International*, 2752876.

Zhao, S. Z., Chung, F., Hanna, D. B., Raymundo, A. L., Cheung, R. Y., & Chen, C. (2004). Dose-response relationship between opioid use and adverse effects after ambulatory surgery. *Journal of Pain and Symptom Management, 28*(1), 35–46.

DÜSTAD
Dünya Sağlık ve Tabiat Bilimleri Dergisi
JOGHENS
Journal of Global Health & Natural Science
ISSN: 2687-637X Yıl: 2022 Cilt: 5 Sayı: 1

The Effect of Bellis on Levels of Plasma Paraoxonase Activity, High-Density Lipoprotein and Malondialdehyde in *Cyprinus carpio L.*, 1758

Akram Mudher Kareem ALJUBOURI[1]
Haci Ahmet DEVECİ[2]
Gökhan NUR[3]

Abstract: The aim of this study is to investigate the effect of Bellis, which is used as a fungicide, on the levels of plasma paraoxonase activity (PON), high-density lipoprotein (HDL), and malondialdehyde (MDA) in *Cyprinus carpio*. A total of 24 (200-300 g) *C. carpio* fish including eight in each group were used. Fish were divided into three groups; Group I (control), Group II (0.025 mg/L Bellis), and Group III (0.050 mg/L Bellis). Blood samples were collected from the fish after 14-day application and their plasmas were separated. Plasma samples were analyzed for PON activity, HDL, and MDA levels. The study findings revealed that PON activity and HDL levels were significantly higher ($p<0.001$) in Group I, compared to Group II and Group III; whereas, MDA levels were lower ($p<0.05$). When the dosage of fungicide increased, PON activity and HDL levels dropped but MDA levels increased. In according to these findings, it was concluded that Bellis, which has been widely used in recent years, may trigger oxidative stress in fish depending on the increasing dose.

Keywords: bellis, *Cyprinus carpio*, malondialdehyde, oxidative stress, paraoxonase activity

Cyprinus carpio L., 1758'de Bellis'in Plazma Paraoksonaz Aktivitesi, Yüksek Dansiteli Lipoprotein ve Malondialdehit Düzeyleri Üzerine Etkisi

Özet: Bu çalışmada, fungusit olarak kullanılan Bellis'in *Cyprinus carpio*'da plazma paraoksonaz aktivitesi (PON), yüksek dansiteli lipoprotein (HDL) ve malondialdehit (MDA) düzeylerine etkisinin araştırılması amaçlandı. Her grupta 8 adet olmak üzere toplam 24 adet (200-300 g) *C. carpio* kullanıldı. Balıklar Grup I (kontrol), Grup II (0,025 mg/L Bellis) ve Grup III (0,050 mgl/L Bellis) olmak üzere üç gruba ayrıldı. 14 günlük uygulamanın ardından balıklardan kan örneği alındı ve plazmaları ayrıldı. Elde edilen plazma örneklerinde PON aktivitesi, HDL ve MDA düzeyleri çalışıldı. Çalışmada elde edilen bulgulara göre Grup I'de PON aktivitesi ve HDL düzeyleri Grup II ve Grup III'e göre anlamlı şekilde ($p<0,001$) daha yüksek bulunurken, MDA düzeyleri ise daha düşük bulundu ($p<0,05$). Fungisit uygulanan balıklarda artan doza bağlı olarak PON aktivitesi ve HDL düzeyleri azalırken MDA düzeylerinin ise arttığı tespit edildi. Bu sonuçlara göre son yıllarda yaygın bir şekilde kullanılan Bellis'in artan doza bağlı olarak balılarda oksidatif stresi tetikleyebileceği sonucuna varıldı.
Anahtar kelimeler: bellis, *Cyprinus carpio*, malondialdehit, oksidatif stres, paraoksonaz aktivite

[1] Department of Pharmacy Technology, Northern Technical University, Mosul, Iraq, akramaljubouri@ntu.edu.iq, 0000-0002-7978-0323.
[2] Department of Biochemistry and Technology, Faculty of Science and Arts, Gaziantep University, Gaziantep, Turkey, h.ahmet_deveci@hotmail.com, 0000-0002-3862-1991.
[3] Corresponding author, Department of Biomedical Engineering, Faculty of Engineering and Natural Sciences, Iskenderun Technical University, Hatay, Turkey, gokhan.nur@iste.edu.tr, 0000-0002-5861-8538.

INTRODUCTION

Since the twentieth century, the natural environment and human health have begun to be adversely affected as a result of excessive application of pesticides. Pesticides used to control agricultural pests can persist in the soil for an extended time period without decomposing and cause detrimental effects on other living beings in the environment (Abdollohi et al., 2004; Deveci et al., 2017; Dogan et al., 2021). These pesticides, which do not decompose in the soil, migrate through the food chain and accumulate in a variety of living beings, resulting in bioconcentration. As they migrate through the food chain, these accumulations reach a higher concentration at each stage. Pesticides and breakdown products that penetrate the body through the food chain eventually have negative impacts on tissues and organs in the course of time (Deveci et al., 2015; Strungaru et al., 2019; Kayhan, 2020).

Fungicides are a type of pesticide that is frequently used in agricultural lands to control pathogenic fungi on plants. Fungicides are used to treat and preserve maize, wheat, olive, pistachio, and fruit, as well as other plants (Chen et al., 2008; Avenot et al., 2008; Temiz, 2019). Bellis® is one of the pesticides that have been increasingly used in recent years in Turkey, particularly in and around Gaziantep, to control pistachio, olive, and pomegranate pests. Bellis® contains anilide and strobilurin (25.2% Boscalid + 12.8% Pyraclostrobin, WG). Boscalid is a novel broad-spectrum fungicide that belongs to the anilide family of fungicides. Its action mode and range are different from those of strobilurins and most the other fungicides. Boscalid inhibits complex II in the mitochondrial electron transport chain; whereas, pyraclostrobin inhibits the complex III (Avenot et al., 2008; Lagunas-Allué et al., 2015; Ozkılınc and Kurt, 2017; Aksakal, 2020).

Fish are used as indicators to identify pollution in the aquatic ecosystem (pesticides, heavy metals, and other chemicals) and its impact on other living beings (Van der Oost et al., 2003; Temiz, 2019). Many environmental factors increase the number of oxidant molecules in living beings by stimulating reactive oxygen species (ROT) (Li et al., 2011; Deveci et al., 2021). Lipid peroxidation, which occurs as the result of pesticide toxicity, causes cellular damage to cells by affecting their antioxidant system. Malondialdehyde (MDA), a product of lipid peroxidation, is a significant indicator of oxidative stress (Kehrer, 1993). Cells activate their antioxidant defense mechanisms to neutralize the harmful effects of oxidative stress induced by oxidant molecules. Catalase (CAT), superoxide dismutase (SOD), glutathione-S-transferase (GST), and glutathione peroxidase (GSH-Px) are the primary defensive mechanisms in fish (Kayhan, 2020). Paraoxonase enzyme (PON), a calcium-dependent esterase enzyme synthesized in the liver, is transported in the serum bound to high-density lipoproteins (HDL). PON acts as an antioxidant by protecting low-density lipoprotein (LDL) from oxidation and neutralizing hydrogen peroxide and other free radicals (Costa et al., 2003; Deveci and Karapehlivan, 2018). PON has been extensively evaluated in toxicological studies in recent years due to its ability to hydrolyze organophosphate pesticides and nerve gases.

The aim of this study is to investigate the effects of Bellis, an important fungicide that has been increasingly used in recent years, on the plasma PON activity, HDL, and MDA levels in *C. carpio.*

MATERIALS and METHODS

In this study, a total of 24 *C. carpio* weighing 200-300 grams that were caught in the İslahiye Tahtaköprü Dam Lake were used. The fish were taken to the laboratory and they were kept in polyethylene tanks for five days to adapt to their new habitat. They were separated into three groups including eight fish in each group following their adaptation to the new habitat. In the control group, Group I, normal water was supplied to the fish's tanks without adding any substance. The fish in

Group II were kept in tanks treated with 0.025 mg/L Bellis® (25.2 % Boscalid + 12.8 % Pyraclostrobin, BASF TURK), whereas the fish in Group III were kept in tanks treated with Bellis® at a dosage of 0.050 mg/L. Given the absorption and evaporation factors of the fungus by the fish, water was changed daily and new dosages were introduced (APHA, 1981). At the end of the fourteenth day, blood samples were drawn from the caudal vein of the fish. Plasma was obtained from blood samples by centrifuging them at 3000 rpm for 10 minutes and kept at -20 °C until analysis began. Plasma PON activity was measured spectrophotometrically according to the method by Eckerson et al., (1983). MDA levels were measured colorimetrically in the spectrophotometer according to the methods described by Yoshoiko et al., (1979). Commercial kits were used to measure HDL levels in an autoanalyzer.

Statistical Analysis

The SPSS 21.0 package software was used to conduct a statistical analysis of the data. The one-way analysis of variance (One Way ANOVA) was employed to determine if there were differences between the groups in terms of PON, HDL, and MDA. Post-hoc (Tukey LSD) analysis was conducted to determine which groups had a significant difference. The results are expressed as mean ± standard deviation ($\bar{x}$±SD). The value of $p<0.05$ was considered statistically significant.

FINDINGS

Table 1 shows the plasma analysis results from fish (Groups II and III) and control (Group I) after 0.025 and 0.05 mg/L Bellis fungicide was added to their tanks for the experimental study, as well as the changes in their parameters.

Table 1. Comparison of PON, HDL, and MDA levels in *C. carpio* with and without Bellis.

Parameters	Group I (Control) mean±SD	Group II (0.025 mg/L) mean±SD	Group III (0.050 mg/L) mean±SD	p
PON (U/L)	29.86±3.66[a]	20.07±2.36[b]	18.55±1.96[b]	<0.001
HDL (mg/dL)	36.42±2.44[a]	29.57±2.44[b]	26.85±2.99[b]	<0.001
MDA (μmol/L)	1.47±0.13[b]	1.74±0.25[a]	1.83±0.24[a]	<0.05

[a, b] The values denoted by different letters on the same line are statistically different. SD: Standard deviation.

When plasma samples from Group I fish that was not been treated were compared with plasma samples from Group II and Group III fish that was treated with, respectively, 0.025 mg/L and h 0.050 mg/L fungicide, the PON activity, and HDL levels were significantly higher ($p<0.001$). When the MDA levels of the control group and the other groups (Group II and Group III) were compared, it was determined that the control group had a statistically significantly lower MDA level ($p<0.05$) (Fig. 1).

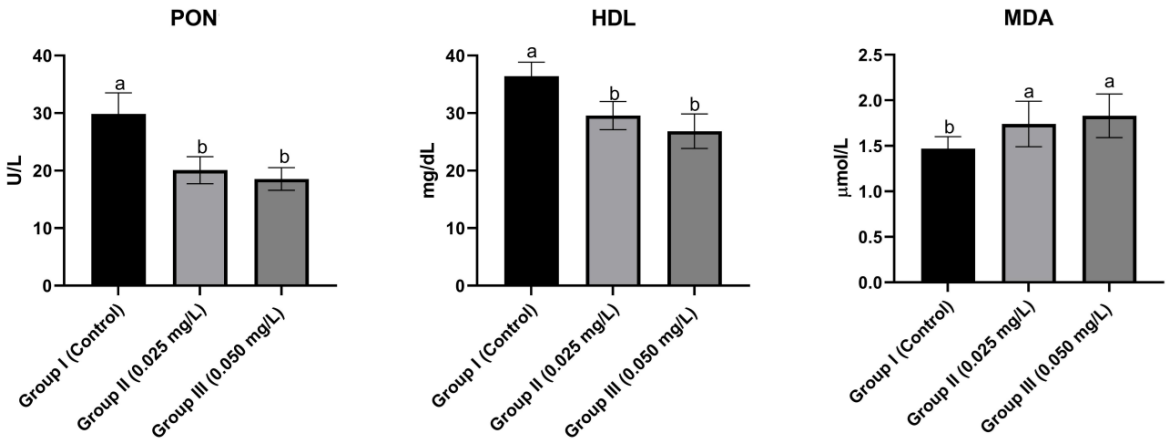


Figure 1. Schematic representation of the PON, HDL, and MDA levels of the groups. [a, b] The values indicated with different letters between different groups are statistically different.

DISCUSSION and CONCLUSION

In parallel to agricultural advancements, the use of pesticides has become significantly widespread to increase both the quantity and quality of the product. Along with being extremely effective in agricultural pest control, pesticides have a detrimental effect on ecosystem health as a result of their long-term and unconscious usage (Çelik et al., 2020; Kaya et al., 2012). Particularly, the contamination of groundwater and other water resources with pesticides poses a potential threat to lifeforms in the aquatic ecosystem. Fish have been extensively employed in recent years to determine the toxicity of the aquatic ecosystem and to predict the possible impacts of agricultural chemicals on other creatures (Selvi et al., 2004; Kaya et al., 2014; Deveci et al., 2017).

Determining the effects of Bellis, which is used intensively in the control of various pests in agricultural lands, on PON, HDL, and MDA levels in fish is important in terms of using pesticides at the appropriate level and minimizing environmental pollution. Additionally, determining the effects of this fungicide on fish enables the prediction of metabolic alterations that may develop in other organisms that ingest these fish. Despite our comprehensive literature review, we have not encountered any study examining the effects of Bellis on PON activity, HDL and MDA levels, this study has an original quality to provide data for other studies. In this regard, this study will serve as a valuable reference for future studies.

Some studies reported that pesticide treatments in fish induced oxidative stress in fish by increasing reactive oxygen species (ROS) in their cells and tissues (Yonar and Sakin, 2011; Deveci et al., 2017; Nur and Deveci, 2018). Oxidative stress negatively affects life by causing genotoxic effects, lipid peroxidation and enzyme inhibitions. Lipid peroxidation, which occurs as a result of the toxic effects of pesticides, is an important indicator of oxidative stress and can be demonstrated by measuring MDA levels (Fırat and Aytekin, 2018; Toroser et al., 2007).

In a study using boscalid, the active component in Bellis, it was reported that while there was an increase in MDA levels depending on the increasing dose of active substance, there was a decrease in the levels of antioxidant enzymes SOD and GST and a significant increase in the CAT level at high doses (Aksakal, 2020). In their study in which they examined the toxic effect of boscalid on zebrafish, Zang et al., (2017) reported that GPx, SOD, CAT, and MDA levels changed based on the boscalid concentration and exposure time. According to the same study, the increase in antioxidant enzyme

activity on the seventh day was a reaction to oxidative stress, and the level of MDA increased significantly after the 21-day treatment. Similarly, the studies utilizing different pesticides reported that MDA, a product of lipid peroxidation, increased in fish blood and different tissues (Durmaz et al., 2006; Isik and Celik, 2008; Deveci et al., 2016; Dogan et al., 2021). MDA levels increased in fish treated with different dosages of Bellis fungicide in the present study, similar to the fish studies conducted with different pesticides above.

The antioxidant properties of the PON enzyme, which is synthesized in the liver and transported depending on HDL, are due to its ability to protect HDL and LDL from oxidation. However, the PON enzyme was reported to be sensitive to oxidative stress and to be subjected to activity loss depending on the increasing oxidant levels (Costa 2003; Deveci et al., 2015; Deveci and Karapehlivan, 2018). A study reported that in trout exposed to different dosages of the organophosphate pesticide glyphosate, the total oxidant level rose depending on dose increase but the total antioxidant level and PON activity decreased (Nur and Deveci, 2018). In their study, Atamanalp et al., (2021) also administered N-acetyl cysteine, an antioxidant, to the fish to which pesticides were applied. They reported that pesticide exposure increased the activities of SOD, CAT, GPx, and PON in all tissues in the group to which the N-acetyl cysteine was administered (Atamanalp et al., 2021). Similar to other studies, the present study revealed a decrease in PON activity and HDL levels in fish treated with different dosages of Bellis fungicide. We think that the decrease in PON activity and HDL levels can be associated with oxidative stress induced by lipid peroxidation of Bellis fungicide.

In conclusion, in the light of the data of the present study, it is considered that Bellis may induce oxidative stress in aquatic organisms, hence causing metabolic alterations in other creatures that ingest these organisms.

Conflict of interest: There is no conflict of interest among the authors.

REFERENCES

Abdollahi, M., Mostafalou, S., Pournourmohammadi, S., & Shadnia, S. (2004). Oxidative stress and cholinesterase inhibition in saliva and plasma of rats following subchronic exposure to malathion. *Comparative Biochemistry and Physiology Part C: Toxicology & Pharmacology, 137(1*), 29-34.

Aksakal, F. I. (2020). Evaluation of boscalid toxicity on *Daphnia magna* by using antioxidant enzyme activities, the expression of genes related to antioxidant and detoxification systems, and life-history parameters. *Comparative Biochemistry and Physiology Part C: Toxicology & Pharmacology, 237*, 108830.

APHA. 1981. Standard methods for the examination of water and wastewater (15th edition), Washington, ISBN: 0875530915, American Public Health Association -Washington, DC, USA.

Atamanalp, M., Parlak, V., Özgeriş, F. B., Yeltekin, A. Ç., Ucar, A., Keleş, M. S., & Alak, G. (2021). Treatment of oxidative stress, apoptosis, and DNA injury with N-acetylcysteine at simulative pesticide toxicity in fish. *Toxicology Mechanisms and Methods, 31(3),* 224-234.

Avenot, H., Morgan, D. P., & Michailides, T. J. (2008). Resistance to pyraclostrobin, boscalid and multiple resistance to Pristine® (pyraclostrobin + boscalid) fungicide in *Alternaria alternata* causing Alternaria late blight of pistachios in California. *Plant Pathology, 57,* 135-140.

Chen, P. J., Moore, T., & Nesnow, S. (2008). Cytotoxic effects of propiconazole and its metabolites in mouse and human hepatoma cells and primary mouse hepatocytes. *Toxicology in Vitro, 22,* 1476-1483.

Costa, L. G., Cole, T. B., Jarvik, G. P., & Furlong, C. E. (2003). Functional genomics of the paraoxonase (PON1) polymorphisms: effects on pesticide sensitivity, cardiovascular disease, and drug metabolism. *Annu Rev Med, 54,* 371-392.

Çelik, Y., Yarşi, G., & Özarslandan, A. (2020). Effects of beneficial bacteria applications on plant yield and resistance mechanisms. *Journal of Global Health & Natural Science, 3(1),* 37-44.

Deveci, H. A., Karapehlivan, M., Kaya, I., Kükürt, A., & Alpay, M. (2015). Akut klorprifos-etil zehirlenmesine karşı kafeik asit fenetil ester'in koruyucu etkisi. *Ankara Üniv Vet Fak Derg, 62,* 255-260.

Deveci, H. A., Kükürt, A., Nur, G., & Kaya, I. (2016). *Cyprinus carpio* (L. 1758)'da klorprifos-etil uygulamasının sialik asit, malondialdehit ve nitrik oksit düzeylerine etkisi. *Kafkas Üniversitesi Fen. Bil. Enst. Derg. 9(2),* 46-51.

Deveci, H. A., Ünal, S., Karapehlivan, M., Ayata, M. K., Gaffaroğlu, M., Kaya, İ., & Yılmaz, M. (2017). Effects of glyphosate (herbicide) on serum paraoxonase activity, high density lipoprotein, total antioxidant and oxidant levels in Kars Creek Transcaucasian Barbs (*Capoeta capoeta* [Guldenstaedt, 1773]). *Fresenius Environmental Bulletin, 26(5),* 3514-3518.

Deveci, H. A., & Karapehlivan, M. (2018). Chlorpyrifos-induced parkinsonian model in mice: Behavior, histopathology and biochemistry. *Pesticide Biochemistry and Physiology, 144*, 36-41.

Deveci, H. A., Nur, G., & Kılıçle, P. A. (2021). Subakut malathion uygulamasının oksidatif stres biyobelirteçlerine etkisi. *J Adv VetBio Sci Tech, , 6(3),* 193-201.

Dogan, D., Deveci, H. A., & Nur, G. (2021). Manifestation of oxidative stress and liver injury in clothionidin exposed *Oncorhynchus mykiss*. *Toxicology Research, 10(3),* 501-510.

Durmaz, H., Sevgiler, Y., & Üner, N. (2006). Tissue-specific antioxidative and neurotoxic responses to diazinon in *Oreochromis niloticus*. *Pesticide Biochemistry and Physiology, 84(3),* 215-226.

Eckerson, H. W., Romson, J., Wyte, C., & La Du, B. (1983). The human serum paraoxonase polymorphism: identification of phenotypes by their response to salts. *American Journal of Human Genetics, 35(2),* 214.

Fırat, Ö., & Aytekin, T. (2018). Neonikotinoid insektisit Thiamethoxam'ın *Oreochromis niloticus*'ta oksidatif stres parametreleri üzerine etkisi. *Balıkesir Üniversitesi Fen Bilimleri Enstitüsü Dergisi, 20(2),* 224-234.

Isik, I., & Celik, I. (2008). Acute effects of methyl parathion and diazinon as inducers for oxidative stress on certain biomarkers in various tissues of rainbow trout (*Oncorhynchus mykiss*). *Pesticide Biochemistry and Physiology, 92(1),* 38-42

Kaya, İ., Karapehlivan, M., Yilmaz, M., Ersan, Y., & Koç, E. (2012). Investigation of effects on plasma nitric oxide, malondialdehyde and total sialic acid levels of glyphosate in Kars Creek Transcaucasian barb (*Capoeta capoeta* [Guldenstaedt, 1773]) in Turkey. *Fresenius Environ Bull, 21(1A),* 123-6.

Kaya, İ., Yilmaz, M., Koç, E., Deveci, H. A., Ersan, Y., & Karapehlivan, M. (2014). Tebukonazol (fungusit) uygulanan *Cyprinus carpio* (L. 1758)'da serum total antioksidan, oksidan ve sialik asit düzeylerinin incelenmesi. *Journal of Fisheries Sciences com, 8(3*), 214.

Kayhan, F. E. (2020). İnsektisitlerin doğadaki döngüsü ve sucul çevreye etkileri. *SU. Fen Fak. Fen Derg, 46(2),* 29-40.

Kehrer, J. P. (1993). Free radicals as mediators of tissue injury and disease. *Critical Reviews in Toxicology, 23(1),* 21-48.

Lagunas-Allué, L., Sanz-Asensio, J., & Martínez-Soria, M. T. (2015). Mobility and distribution of eight fungicides in surface, skin and pulp in grapes. An application to pyraclostrobin and boscalid. *Food Control, 51,* 85-93.

Li, Z. H., Zlabek, V., Velisek, J., Grabic, R., Machova, J., Kolarova, J., Li, P. & Randak, T. (2011). Antioxidant responses and plasma biochemical characteristics in the freshwater rainbow trout, *Oncorhynchus mykiss*, after acute exposure to the fungicide propiconazole. *J Anim Sci, 56*, 61-69.

Nur, G., & Deveci, H A. (2018). Histopathological and biochemical responses to the oxidative stress induced by glyphosate-based herbicides in the rainbow trout (*Oncorhynchus mykiss*). *Journal of Cellular Neuroscience and Oxidative Stress, 10(1*), 656-665.

Ozkılınc, H., & Kurt, S. (2017). Screening fungicide resistance of alternaria pathogens causing Alternaria blight of pistachio in Turkey. *YYÜ Tar Bil Derg, 27(4),* 543-549.

Selvi, M., Sarıkaya, R., & Erkoç, F. (2004). Acute behavioral changes in the guppy *(Poecilia reticulata)* exposed to temephos. *Gazi Üniversitesi Fen Bilimleri Dergisi, 17,* 15-19.

Strungaru, S. A., Plavan, G., Ciobica, A., Nicoara, M., Robea, M. A., Solcan, C., & Petrovici, A. (2019). Toxicity and chronic effects of deltamethrin exposure on zebrafish (*Danio rerio*) as a reference model for freshwater fish community. *Ecotoxicology and Environmental Safety, 171,* 854-862.

Temiz, Ö. (2019). *Oreochromis niloticus*'un karaciğerinde fungisit propiconazole'un oksidatif stres parametreleri ve antioksidan sistem enzimleri üzerine etkileri. *Journal of Anatolian Environmental and Animal Sciences, 4(1),* 43-47.

Toroser, D., Orr, WC., & Sohal, R. S. (2007). Carbonylation of mitochondrial proteins in *Drosophila melanogaster* during aging. *Biochemical and Biophysical Research Communications, 363*, 418-424.

Van der Oost, R., Beyer, J., & Vermeulen, N. P. E. (2003). Fish bioaccumulation andbiomarkers in environmental risk assessment: a review. *Environ Toxicol Pharmacol, 13,* 57-149.

Yonar, M. E., & Sakin, F. (2011). Ameliorative effect of lycopene on antioxidant status in *Cyprinus carpio* during pyrethroid deltamethrin exposure. *Pesticide Biochemistry and Physiology, 99*, 226-231.

Yoshioka, T., Kawada, K., Shimada, T., & Mori, M. (1979). Lipid peroxidation in maternal and cord blood and protective mechanism against activated oxygen toxicity in the blood. *American Journal of Obstetrics & Gynecology, 135,* 372-376.

Zang, X., Ji M, Wang, K., Li, X., Zhang, Y., Li, X., Tian, H., Zhu, H., & Du, F. (2017). Effects of boscalid on the antioxidant enzyme system of adult zebrafish (*Danio rerio*). *Agricultural Science & Technology, Animal Science and Feeds, 18(2),* 287-293.

DÜSTAD
Dünya Sağlık ve Tabiat Bilimleri Dergisi
JOGHENS
Journal of Global Health & Natural Science
ISSN: 2687-637X Yıl: 2022 Cilt: 5 Sayı: 1

Evaluation of Patients Hospitalized in an Internal Diseases Clinic During the Pandemic Period

Arzu Cennet IŞIK[1]
Sena YAZICI ALCAN[2]
Mehmet Emirhan IŞIK[3]
Özcan KESKIN[4]

Abstract: Internal medicine clinics offer solutions to important problems of the health system such as the management of chronic diseases and further examination of undiagnosed conditions, besides the acute problems of patients. In addition to treating COVID-19 patients during the pandemic period, they continued their current duties and showed that they are an important part of the health system. In our study, we aimed to evaluate the demographic characteristics, reason and duration of hospitalization, and survival rates of patients hospitalized in the internal medicine clinic of a city hospital during the third wave of the pandemic. The study is a retrospective, descriptive and includes patients between 01.10.2021 and 31.12.2021 cross-sectionally. The files of 262 hospitalized patients in our clinic during this period were analyzed and included in the study. Age, gender, clinical diagnosis, length of hospital stay, comorbid disease status, COVID-19 disease and vaccination history of the patients were recorded. The mean age of the patients was 63.3±6.3, and the number of patients over 65 years was 149 (57%). The number of male and female patients was equal (131/131). Hypertension was the most common disease associated with hospitalization diagnoses. This was followed by diabetes mellitus, ischemic heart disease, chronic kidney disease, malignancies, and chronic liver disease, respectively. The patients with the most common upper gastrointestinal bleeding were hospitalized. Anemia examination and malignancy screening patients followed this up. The rate of history of COVID-19 disease was 18.7% and the vaccination rate was 92%. Internal medicine clinics are a major branch in which the general approach is very important, and which aims to get the most efficient result by working in coordination with other departments in the shortest time with a holistic, multisystemic and analytical way of thinking. The importance of internal medicine clinics has come to the fore once again during the pandemic period.

Keywords: internal diseases, hypertension, gastrointestinal bleeding, diabetes mellitus, malignancy

Pandemi Döneminde Bir İç Hastalıkları Kliniğinde Yatan Hastaların Değerlendirilmesi

Özet: Dahiliye klinikleri, hastaların akut sorunlarının yanı sıra, kronik hastalıklarının yönetimi ve tanı almamış durumların ileri incelenmesi gibi sağlık sisteminin önemli sorunlarına çözüm sunmaktadırlar. Pandemi döneminde de COVID-19 hastalarının tedavi edilmesinin yanında mevcut görevlerine devam etmişler ve sağlık sisteminin

[1] Corresponding author, MD University of Health Sciences, Kartal City Hospital, Department of Internal Medicine-İstanbul/Türkiye, arzukaracelik@gmail.com, 0000-0001-9844-8599.
[2] MD, University of Health Sciences, Sancaktepe Prof. İlhan Varank training and Research Hopital, Department of Internal Medicine-İstanbul/Türkiye, drsenayzc@gmail.com, 0000-0001-8843-9613.
[3] MD, University of Health Sciences, Koşuyolu High Specialization Training and Research Hospital, Department of Infectious Diseases, emirhan82@gmail.com, 0000-0002-0699-8890.
[4] Prof. Dr., University of Health Sciences, Kartal City Hospital, Department of Internal Medicine, okekskin34@yahoo.com, 0000-0002-9562-6967

önemli bir parçası olduklarını göstermişlerdir. Çalışmamızda pandeminin üçüncü dalgası sırasında bir şehir hastanesinin iç hastalıkları kliniğine yatan hastaların demografik özellikleri, yatış neden ve süreleri ile sağkalım oranlarının değerlendirilmesini amaçladık. Araştırmamız retrospektif tipte, tanımlayıcı bir çalışma olup, kesitsel olarak 01.10.2021 ve 31.12.2021 tarihleri arasındaki hastaları kapsamaktadır. Kliniğimizde bu dönemde yatan 262 hastanın dosyası incelenip, çalışmaya dahil edildi. Hastaların yaş, cinsiyet, klinik tanıları, hastanede yatış süresi, komorbid hastalık durumu, COVID-19 hastalığı ve aşısı öyküsü bilgileri kaydedildi. Hastaların yaş ortalaması 63.3±6.3 ve 65 yaş üzeri hasta sayısı 149 (57%) olarak saptandı. Kadın ve erkek hasta sayısı eşitti (131/131). Yatış tanılarına eşlik eden hastalıklarda en sık hipertansiyon görülmekteydi. Bunu sırasıyla, diabetes mellitus, iskemik kalp hastalığı, kronik böbrek hastalığı, maligniteler ve kronik karaciğer hastalığı izlemekteydi. En sık üst gastrointestinal sistem kanaması nedeniyle yatış yapıldı. Anemi tetkik ve malignite tarama hastaları bunu izledi. COVID-19 hastalığı geçirme oranı %18,7 ve aşı yaptırma oranı %92 olarak belirlendi. İç hastalıkları klinikleri genel yaklaşımın çok önemli olduğu; bütüncül, multisistemik ve analitik düşünce tarzıyla en kısa sürede diğer bölümlerle koordine çalışıp en verimli sonucu almayı hedefleyen bir ana daldır. İç hastalıkları kliniklerinin önemi pandemi döneminde bir kez daha ön plana çıkmıştır.

Anahtar kelimeler: iç hastalıkları, hipertansiyon, gastrointestinal sistem kanaması, diyabetes mellitus, malignite

INTRODUCTION

Internal medicine practice is a discipline that requires a general and comprehensive approach to the patient as a branch where the patient density is higher than outpatients and inpatients. Coronavirus disease 2019 (COVID-19) pandemic has once again demonstrated how important internal medicine clinics are. The need for hospital beds has also increased during the pandemic given that both COVID-19 patients and patients with chronic diseases, especially geriatrics, continue to be hospitalized. It is important to plan the necessary examinations and treatments for the current diseases and preliminary diagnosis of inpatients. The leading chronic diseases are diabetes mellitus (DM), hypertension (HT), chronic kidney failure (CKD) and malignancies. While the pandemic continues, these diseases have not disappeared, on the contrary, the control of these diseases has become more difficult with the decrease in routine controls.

Patients are frequently hospitalized from emergency and outpatient clinics to ensure blood sugar regulation (Levetan & Magee, 2000). While some of these hospitalized patients have been diagnosed with diabetes before, some of them are diagnosed during hospitalization (Clement et al., 2004). Diabetes mellitus ranks in top four in frequency among the non-communicable diseases, which are the main cause of death in our country as it is in the world. According to the TURDEP-II study, 42% of the adult population in Turkey is diabetic or prediabetic (Satman et al., 2013). In the study of Umpierrez et al., in which they screened 2030 hospitalized patients, the frequency of hyperglycemia was found to be 38%, and they observed that 26% of the patients had diabetes mellitus (DM), while 12% had no history of DM (Umpierrez et al., 2002). HT is a common disease related with many branches. 30% of the population is unaware that they are hypertensive, and 65% of the diagnosed patients have poor control (Lapidus et al., 2021). The prevalence of age-standardized HT calculated for 2020, based on TURDEP-II data, was 29.6% (Satman et al., 2013). About half (47%, or 116 million) of adults in the United States have HT, defined as systolic blood pressure greater than 130 mmHg or diastolic blood pressure greater than 80 mmHg, and are taking medications for it (Centers for Disease Control and Prevention, 2021).

In a study conducted in the United States between 2015 and 2018, 14.9% of the United States adult population was found to have low eGFR or proteinuria. Although the prevalence of CKD decreased in a few risk groups, including elderly individuals, those with diabetes, hypertension, and cardiovascular disease, the number remained stable due to the increase in these diseases in the population (Bethesda, 2020). Epidemiological studies on CKD from different countries have yielded related results. According to the results of these studies, the rate of CKD in the world varies between 10-16%, and the rate of

microalbuminuria varies between 6-14% (Bello et al., 2015; Hallan et al., 2006). The Chronic Renal Disease in Turkey (CREDIT) study, which included 10,748 individuals over the age of 18 in 23 provinces in Turkey, determined that the prevalence of CKD in the general adult population in Turkey was 15.7%. In adults, the rate of microalbuminuria, which is an indicator of kidney damage, was found to be 10.2%, and the rate of macro albuminuria was 2%. It proves that CKD is an important public health problem in Turkey as it is in the world (Süleymanlar et al., 2011). The number of patients with malignancy is increasing all over the world. Especially the increase in elderly patients and diagnosis opportunities contribute to this increase. Although there are advances in treatment possibilities, the management of side effects of oncological treatments, such as chemotherapy and radiotherapy are also difficult. The Global Cancer Observatory (GLOBOCAN) 2020 provides estimates of incidence and mortality rates for 36 cancer types from 185 countries and for all cancer types for 2020. In the light of these data, it was reported that the global cancer burden increased to 19.3 million new cases and 10.0 million deaths in 2020 (World Health Organization, 2020).

In our study, we aimed to evaluate the demographic data, reasons for hospitalization, hospitalization duration, and survival rate of patients hospitalized in the internal medicine clinic of a city hospital during the third wave of the pandemic.

MATERIALS and METHODS

The study is a retrospective, descriptive and cross-sectional and includes information about the patients hospitalized in the internal medicine clinic between 01.10.2021 and 31.12.2021. Patient information was obtained from the hospital electronic records and the "e-Nabız" of the Ministry of Health. The files of 262 hospitalized patients were analyzed and included in the study. Patients' age, gender, diagnosis, length of hospital stay, comorbid disease, COVID-19 history, and vaccine status were recorded. Diseases previously confirmed by a health institution were considered comorbidities, and inpatient diagnoses were accepted as new diagnoses. The length of stay in the hospital covers the period from the day when the patient is admitted to discharge (death, discharge, or transfer to a different unit). In the evaluation of the length of stay, 1-10 days were noted as ordinary, while cases exceeding 10 days were considered as prolonged hospitalization. Among the patients who were transferred between clinics, the time from the day they were admitted to the time they left the clinic was taken as the basis. COVID-19 and vaccination history were evaluated by patient statement and confirmed via the e-Nabız system.

Patients are accepted from the emergency room, outpatient clinic, and by in-hospital transfer. Patients who applied to the emergency service and who were consulted to our department, are evaluated, and followed up in the internal medicine inpatient clinic. Hospitalization is planned for patients who are in the internal diseases' polyclinic application process, in the case they require further examination. Patients taken from other clinics with inpatient services other than internal diseases are accepted as in-hospital transport when the disease process is completed with the relevant branch because of consultation and evaluation.

Microsoft Excel was used in the analysis of the data. Numerical data were expressed as mean standard deviation, categorical data as percentage. In the analysis of the data, mean age was calculated together with its standard deviations. The reasons for hospitalization were taken from the database and divided in groups. Since some patients had more than one reason for hospitalization, the total rate was not calculated as 100 percent.

Ethics committee approval was obtained from the ethics committee of University of Health Sciences, Kartal Dr. Lütfi Kırdar City Hospital on 28.01.2022 with the decision number 2022/514/218/17.

RESULTS

A total of 262 patients who were hospitalized in our internal medicine clinic between 01.10.2021 and 31.12.2021 were included in the study. The mean age of the patients was 63.3±6.3, and the number of patients over 65 was 149 (57%). The number of female and male patients was equal (131/131). The conditions accompanying the hospitalization diagnoses of the patients were most frequently hypertension 57% (n: 150) and followed by diabetes mellitus 40% (n: 105), ischemic heart disease 45% (n: 118), chronic renal disease 26% (n: 68), malignancy 14% (n: 37), and chronic liver disease 4% (n: 11) (Table 1).

Table 1. Demographic features and underlying diseases of patients.

Variables	**N, %**
Age (mean, years, SD)	63.3±6.3
Gender (female)	131 (50)
Length of hospital stay	
0-10 days	223 (85.1)
11-20 days	29 (11)
≥21 days	10 (3.8)
Underlying diseases	
Hypertension	150 (57)
Ischemic heart disease	118 (45)
Diabetes mellitus	105 (40)
Chronic kidney disease	68 (26)
Malignancy	37 (14)
Chronic liver disease	10 (11)

The average length of stay of the patients was 6.63±5.27 days, and when the duration of hospital stay was considered, 223 (85.1%) patients were hospitalized between 0-10 days, 29 patients (11%) were hospitalized between 11-20 days. Prerenal and renal-induced acute exacerbation of patients with chronic renal failure and acute renal failure occurred with the highest rate of 44% (n: 115) in hospitalizations exceeding 10 days. 80.2% (n: 210) of the patients from the emergency service admitted to the clinic. In addition, 10.3% (n: 27) of the patients were transferred from other clinics, and 9.5% (n: 25) referred from our polyclinics. After hospitalization, 11 of 13 patients were transferred to the intensive care unit, and nine (82%) of these patients died. Three patients died in the clinic.

The most frequent hospitalization was for upper gastrointestinal (GI) bleeding. This was followed by anemia and malignancy screening patients, respectively. Methyl alcohol intoxication was followed up as at least one patient. The reasons for hospitalization and distribution of the patients are shown in Table 2.

Table 2. Indications of hospitalization.

Indications	N	%
Gastrointestinal bleeding	48	18.3
Anemia	45	17.1
Malignancy	33	12.5
Acute exacerbation of chronic renal failure	28	10.6
Impairment of oral intake and malnutrition treatment	23	8.7
Malignant palliation treatment	22	8.3
Electrolyte Imbalance	15	5.7
Diabetic emergencies, complications, blood sugar regulation	15	5.7
Acute renal injury	14	5.3
Acute liver enzyme elevation	8	3.05
Heart failure treatment	4	1.9
Diabetic foot	3	1.1
Hypertensive emergency (adrenal pathology)	2	0.7
Methyl alcohol intoxication	1	0.3

In the evaluation of the pathology reports of forty-eight patients hospitalized with the diagnosis of GI bleeding, who underwent endoscopic procedure, chronic active/inactive gastritis was found in 75% (n: 32) and gastric malignancy in 12.5% (n: 6). While 12 (25%) patients with bleeding were using acetylsalicylic acid, it was determined that nine patients were receiving new generation anticoagulant therapy. One patient who was hospitalized due to upper GI bleeding died on admission to the ward. Blood transfusion was performed in all forty-five patients hospitalized due to anemia. Malignancy was detected in 19 of 33 patients who were hospitalized with symptoms such as weight loss, presence of mass and loss of appetite and who were screened for malignancy. GI malignancy was detected in seven of these patients, urogenital system insix6 patients and hematological malignancy in five patients. Osteosarcoma was detected in one patient. While the number of patients with chronic liver disease was eleven (4%) before hospitalization, we had four (1.5%) newly diagnosed patients. Five patients (1.7%) were discharged with the diagnosis of type 2 DM during hospitalization.

During the pandemic, the proportion of patients with COVID-19 was 18.7% (n: 49). While 92% (n: 241) of our patients were vaccinated, 65.8% (n: 172) of these patients had mRNA vaccine, 22% (n:58) had inactivated vaccine, and all these patients had mRNA vaccine later. The ratio of patients who were not vaccinated for COVID-19 was 7.6% (n: 20).

DISCUSSION

Hospitalization of patients and providing their treatment are the duty of the health system, and an important part of this is composed of patients hospitalized in the internal medicine clinic (Demircan et al., 2005). Internal medicine clinics are not only areas where acute problems of patients are solved, but also centers where the regulation of chronic diseases is provided. In our study, the most common hospitalization diagnosis was gastrointestinal bleeding, followed by anemia and malignancy examination. Hypertension takes the first place among the chronic diseases of the patients, followed by diabetes mellitus and ischemic heart disease.

Gastroscopy was performed on all hospitalized patients due to GI bleeding. In a study in which 403 patients with upper GI bleeding were evaluated. Duodenal ulcer was found at the rate of 39.2%, and 52.6% of them were using nonsteroidal anti-inflammatory and/or acetylsalicylic acid (ASA) (Yalçın et al., 2016). In a study in which patients with upper GI bleeding were screened, duodenal ulcer was found in 31.2% of 198 patients, gastritis was in the second place with 29.2%, and ASA was the leading cause

of bleeding with a rate of 16.2% (Olt et al., 2015). Chronic/active gastritis was detected in 75% of our patients. When the drug use of our patients followed up with upper GI bleeding was evaluated, it was seen that the most common reason was the use of 25% low dose (81-100 mg) ASA. In a meta-analysis study in which 14 randomized controlled and observational studies were evaluated, low-dose ASA use was associated with an increased risk of upper gastrointestinal bleeding, similar to our results (McQuaid & Laine, 2006).

Hyperglycemia in hospitalized patients is not only seen in diabetic patients. Patients are found to have hyperglycemia while they are examined for DM in the hospital. Even though, 40% of the patients were diagnosed with DM before hospitalization, 5 patients (1.7%) were diagnosed with type 2 DM during hospitalization. In hospitalized patients, 36% (n: 94) were hospitalized for the purpose of blood sugar regulation and approximately one-third of these patients were newly diagnosed diabetes. In addition to all these, high blood sugar has been reported as a factor that causes a prolongation of hospitalization (Gogas Yavuz et al., 2013). The length of stay of diabetics exceeding 10 days is 22%.

The overall prevalence of hypertension generalized by age and gender in Turkey is 31.8%, and the rate is higher in women. The proportion of patients who never had their blood pressure measured was 32.2%, and only 40.7% of those with hypertension were aware of their diagnosis. However, 31.1% of the patients were under pharmacological treatment and only 8.1% of them were able to control their blood pressure. The rate of those who were aware and treated and whose blood pressure was under control was 20.7%. these results show that hypertension is a common but poorly managed health problem in Turkey (Altun et al., 2005; T.C. Sağlık Bakanlığı, 2020). In our data, the most common chronic disease was hypertension with 57%, and the least common was chronic liver disease with 4%. All our HT patients were under medical follow-up, but the awareness rate was low at 18%, like Turkey's overall.

In our study, we observed that patients with acute exacerbation of chronic renal failure and acute renal failure had prolonged follow-up periods in hospitalization. The reason for this is to delay the treatment of patients such as hemodialysis and renal transplantation, which may cause poor prognosis and mortality, while being followed up with renal failure treatments in the acute stage. Normalizing renal functions, examining the factors that may cause failure, controlling additional diseases, side effects of long-term medications, infection status that may develop during hospitalization and patient-related factors are effective in this process. In a study in which 19,982 patients with renal failure were evaluated, it was concluded that acute renal failure is associated with significantly increased mortality, long hospitalization and cost, and its prevention and effective treatment should be a priority in terms of public health (Chertow et al., 2005). In a similar study, it was determined that patients with renal failure who were treated in hospital continue to have a serious health problem. Infection, advanced age, use of contrast matter and medication, oral intake disorder, and history of surgery are more common risk factors. In terms of comorbidities, hypertension, diabetes, and ischemic heart disease are more common. Preservation of renal perfusion, treatment of underlying diseases, regular monitoring of fluid-electrolyte monitoring, and avoidance of nephrotoxic agents remain current in treatment (Ayar et al., 2015). In the follow-up of our patients, the decision of permanent hemodialysis was taken by the nephrology department at a rate of 45%, and these patients were accepted as end-stage acute renal failure patients.

GI tumors were most detected in patients hospitalized for malignancy screening. In 2020, the most frequently detected cancers in our country were order lung, breast, colorectal, prostate, and thyroid cancers. Colorectal cancer is the third most common cancer in both men and women (World Health

Organization, 2020). The rate of diagnosed malignancies in our study was 7.2%, and GI malignancies were in the first place with 36.8% new diagnoses. This was followed by urogenital system malignancy with a rate of 26.3%. Nutritional problems, electrolyte imbalance, and low hemoglobin are the most common signs and symptoms in patients with a diagnosis of malignancy and in advanced geriatric age groups. Symptomatic and palliative support treatments are planned for the symptoms and findings of these patients and their follow-up is provided. In our study, we provided palliative care support to 9.9% of our patients.

In a public health study evaluating vaccine hesitancy/rejection in two different periods before and after the COVID-19 pandemic, most of the websites examined had positive content about the vaccine. Social fear and interest in the COVID-19 vaccine during the pandemic may be an opportunity to reduce the general vaccine hesitancy. Vaccine hesitation/rejection was seen at a rate of 7% and patients stated that they were afraid and did not trust the content of the vaccine. As of the end of February 2022, the rate of those who received the second dose of vaccine in the population aged 18 and over was 85.06%, while the rate of those who received the first dose was 92.92% as reported by the Ministry of Health (T. C. Sağlık Bakanlığı, 2022).

Our population is getting older, and the acute problems of comorbid diseases and chronic problems also accept a lot of space in our daily practice. In addition, with the spread of sub-branch clinics, the discipline of internal medicine is changing. However, patients with multiple organ problems need general evaluation, and internal medicine clinics play a crucial role in the diagnosis process, support, and permanent treatment of patients. For inpatient services, which are important in our health system, it may be useful to determine the financial, personnel and resource needs required by larger and multi-center studies.

CONCLUSION

In internal medicine clinics, a wide range of issues such as patients' acute problems, management of chronic diseases, and detailed examination of undiagnosed conditions are dealt with. The duration of hospitalization, especially in acute attacks of chronic diseases and during examination phases, is prolonged. Affirming that the general internal medicine approach still maintains its importance today, it is imperative to aim for the most efficient results by working in coordination with the minor branches in the shortest time with a holistic, multisystemic and analytical way of thinking.

Limitations

The main limitation for our study is that it was conducted in a single center. It should also be noted that different approaches may differ between clinics in terms of patient admission and follow-up.

Conflict of interest: There is no conflict of interest among the authors.

REFERENCES

Altun, B., Arici, M., Nergizoğlu, G., Derici, Ü., Karatan, O., Turgan, Ç., ... Cağlar, S. (2005). Prevalence, awareness, treatment, and control of hypertension in Turkey (the PatenT study) in 2003. *J Hypertens*, *23*(10), 1817-23.

Ayar, Y., Ersoy, A., Sayılar, E. I., Yavuz, M., Karaduman, R., Bayram, D., … Suveran, M. M. (2015). Üçüncü basamak sağlık merkezinde takip edilen akut böbrek hasarlı hastaların değerlendirilmesi. *Van Tıp Dergisi, 2*(4), 206-215.

Bello, A. K., Levin, A., Manns, B. J., Feehally, J., Drueke, T., Faruque, L., … on behalf of the Kidney Health for Life Initiative. (2015). Effective CKD care in European countries: challenges and opportunities for health policy. *Am J Kidney Dis*, *65*(1), 15–25.

Bethesda, M. (2020). National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases. United States Renal Data System. 2020 USRDS Annual Data Report: Epidemiology of kidney disease in the United States.

Demircan, C., Çekiç, C., Akgül, N., Odabaşı, A., Çalışır, N., Kiyici, S., … Keskin, M. (2005). Acil dahiliye ünitesi hasta profili: 1 yıllık deneyim. *Uludağ Üniversitesi Tıp Fakültesi Dergisi*, *31*(1), 39–43.

Centers for Disease Control and Prevention. (2021). *Facts about hypertension*. https://www.cdc.gov/bloodpressure/facts.htm

Chertow, G. M., Burdick, E., Honour, M., Bonventre, J. V., & Bates, D. W. (2005). Acute kidney injury, mortality, length of stay, and costs in hospitalized patients. *Journal of the American Society of Nephrology*, *16*(11), 3365–3370.

Clement, S., Braithwaite, S. S., Magee, M. F., Ahmann, A., Smith, E. P., Schafer, R. G., … on behalf of the Diabetes in Hospitals Writing Committee. (2004). Management of diabetes and hyperglycemia in hospitals. *Diabetes Care*, *27*(2), 553–591.

Gogas Yavuz, D., Yazici, D., Özcan, S., Tarçin, Ö., DeynelI, O., & Akalin, S. (2013). Hyperglycemia in hospitalized patients. *Marmara Med J*, *26*(2), 68–71.

Hallan, S. I., Coresh, J., Astor, B. C., Asberg, A., Powe, N. R., Romundstad, S., … Holmen, J. (2006). International comparison of the relationship of chronic kidney disease prevalence and ESRD risk. *J Am Soc Nephrol*, *17*(8), 2275–2284.

Lapidus, M. I., Falcón, A., Antonietti, C., & Peuchot, V. (2021). Prevalence of high blood pressure in hospitalized patients. A cross-sectional study. *Medicina (B Aires)*, *81*(6), 1002–1006.

Levetan, C. S., & Magee, M. F. (2000). Hospital management of diabetes. *Endocrinol Metab Clin*, *29*(4), 745–770.

McQuaid, K. R., & Laine, L. (2006). Systematic review and meta-analysis of adverse events of low-dose aspirin and clopidogrel in randomized controlled trials. *Am J Med*, *119*(8), 624–638.

Olt, S., Uslan, İ., Eminler, A. T., Tamer, A., Akçay, E. Ü., Baştemir, A., … Ergenç, H. (2015). Evaluation of patients with upper gastrointestinal bleeding retrospectively. *Sak Med J*, *5*(3), 130–134.

T. C. Sağlık Bakanlığı. (2020). Hipertansiyon klinik protokolü. Sağlık Hizmetleri Genel Müdürlüğü, T. C. Sağlık Bakanlığı Yayın No: 1172.

T. C. Sağlık Bakanlığı. (2022). COVID-19 Bilgilendirme platformu. https://covid19.saglik.gov.tr/

Satman, I., Omer, B., Tutuncu, Y., Kalaca, S., Gedik, S., Dinccag, N., … TURDEP-II Study Group. (2013). Twelve-year trends in the prevalence and risk factors of diabetes and prediabetes in Turkish adults. *Eur J Epidemiol*, *28*(2), 169–180.

Süleymanlar, G., Utaş, C., Arinsoy, T., Ateş, K., Altun, B., Altiparmak, M. R., … Serdengeçti, K. (2011). A population-based survey of Chronic REnal disease in Turkey-the CREDIT study. *Nephrol Dial Transplant*, *26*(6), 1862–1871.

Umpierrez, G. E., Isaacs, S. D., Bazargan, N., You, X., Thaler, L. M., & Kitabchi, A. E. (2002). Hyperglycemia: an independent marker of in-hospital mortality in patients with undiagnosed diabetes. *J Clin Endocrinol Metab, 87*(3), 978–982.

World Health Organization. (2020). The global cancer observatory. https://gco.iarc.fr/

Yalçın, M. S., Kara, B., Öztürk, N. A., Ölmez, Ş., Taşdoğan, B. E., & Taş, A. (2016). Epidemiology and endoscopic findings of the patients suffering from upper gastrointestinal system bleeding. *Dicle Med J*, *43*(1), 73–76.

DÜSTAD
Dünya Sağlık ve Tabiat Bilimleri Dergisi
JOGHENS
Journal of Global Health & Natural Science
ISSN: 2687-637X Yıl: 2022 Cilt: 5 Sayı: 1

Farklı Bakteri Strainleri (PGPR) Uygulamalarının Marulda (*Lactuca sativa L.)* Fide Gelişimi ve Kalitesi Üzerine Etkileri

Yusuf ÇELİK[1]

Özet: Bitkisel üretimde verim ve kalitenin artırılmasında etkili temel bileşenlerin başında sağlıklı ve kaliteli fide üretimi gelmektedir. Bu çalışma, bitki gelişimini teşvik eden farklı bakteri strainlerinin (Plant Growht Promoting-PGPR) marul fidesi yetiştiriciliğinde, fide gelişimi ve kalitesine etkisini belirlemek amacıyla kontrollü koşullarda yürütülmüştür. Çalışma sonunda; bitki köksüz boyu, bitki gövde çapı, yaprak sayısı, yaprak eni, bitki yaş ve kuru ağırlığı, kök boyu, kök yaş ve kök kuru ağırlığı ölçülmüştür. Farklı bakteri(PGPR) strainlerinin marul fidelerine uygulanmaları sonucunda yapılan ölçümlerde; bitki köksüz boyu, bitki kök uzunluğu, bitki çapı, bitki köksüz yaş ve kuru ağırlığı, bitki kök yaş ve kuru ağırlığı, toplam yaprak sayısı, yaprak eni gibi verim ve kalite parametrelerinin gelişiminde etkili oldukları saptanmıştır. Yapılan ölçüm ve istatistiki analizlere göre tüm bakterilerin kontrol uygulamasına göre daha etkili oldukları görülmüştür. Farklı PGPR strainleri uygulamalarının kontrol uygulamasına göre fide boyunda % 28.7, gövde çapında % 14.1, yaprak çapında % 9, yaprak yaş ağırlığında % 49.5, yaprak sayısında % 11.7 ve kök uzunluğunda % 15,18 oranlarında artış yaptığı saptanmıştır. Sonuç olarak; çalışmada kullanılan bakteri strainlerinin tümü kontrole göre bitki gelişimini artırırken YÖ41 bakteri straini ön plana çıkmıştır. Çalışma sonucunda farklı bakteri uygulamalarının marul fidesi yetiştiriciliğinde kullanılmasının fide gelişimi ve kalitesi üzerinde olumlu etki yaptığı belirlenmiş olup ancak çalışmanın daha da genişletilmesi ve farklı bitki tür ve çeşitlerinde kullanılmasının daha kapsamlı olacağı sonucuna varılmıştır.

Anahtar kelimeler: marul, fide gelişimi, PGPR uygulamaları, kalite

The Effects of Different Bacterial Strains (PGPR) Applications on Seedling Growth and Quality in Lettuce (*Lactuca sativa* L.)

Abstract: Production of healthy and high quality seedlings is one of the main components effective in increasing yield and quality in plant production. This study was carried out under controlled conditions to determine the effects of different bacterial strains (Plant Growht Promoting-PGPR) that promote plant growth on the growth and quality of lettuce seedlings. At the end of the study; Plant rootless height, plant stem diameter, number of leaves, leaf width, plant fresh and dry weight, root length, root fresh and root dry weight were measured. In the measurements made as a result of the application of different bacterial (PGPR) strains to lettuce seedlings; It was determined that they were effective in the development of yield and quality parameters such as plant rootless height, plant root length, plant diameter, plant rootless fresh and dry weight, plant root fresh and dry weight, total leaf number, leaf width. According to the measurements and statistical analyzes, it was seen that all bacteria were effective compared to the control. It was determined that the applications of different PGPR strains increased the seedling length by 28.7%, the stem diameter by 14.1%, the leaf diameter by 9%, the leaf fresh weight by 49.5%, the number of leaves by 11.7% and the root length by 15.18% compared to the control application. As a result, while all of the bacteria used in the application were effective compared to the control, YÖ41 bacterial strain came to the fore. As a result of the study, it was determined that the use of different bacterial applications in lettuce seedlings

[1] Silifke Meslek Yüksekokulu, Bitkisel ve Hayvansal Üretim Bölümü, Mersin Üniversitesi, 33940 Silifke, Mersin, Türkiye, ycelik33@mersin.edu.tr, 0000-0002-8590-6690

had a positive effect on the seedling growth and quality, but it was concluded that the study would be further expanded and used in different plant species and varieties.

Keywords: seedling growth , lettuce, PGPR applications, quality

GİRİŞ

Marul (*Lactucasativa*L.), *Compositae* (*Asteraceae*) familyasının *Lactuca*cinsine ait tek yıllık olarak bilinen serin iklim sebze grubundandır. Marul yaprakları en çok tüketilen sebzelerin başında gelmektedir (Eşiyok 2012). Dünyada uzun yıllardan beri tarımı yapılan ve severek tüketilen marul neredeyse bütün yıl boyunca pazarlarda ve marketlerde yerini almaktadır (Aybak, 2002). Marul çeşit zenginliği en fazla olan sebzeler arasındadır. Ülkemizin hemen her yerinde açıkta veya örtü altında yetiştirilmesi mümkündür. Marul iklim koşullarının elverişli olduğu her dönemde açık arazide yetiştirilebilmektedir. İklim koşullarının uygun olmadığı soğuk kış aylarında örtü altında, yaz aylarında ise yüksek yayla kesimlerinde verim ve kalite bakımından iyi sonuçlar vermektedir (Eşiyok, 2012).

Modern tarım sistemlerinde, başarılı üretimin asli unsurlarından birisi de kaliteli ve nitelikli fide ile yapılan üretimdir. Sebzecilikte fide ile üretim, üretimde avantaj sağlaması nedeni ile çok tercih edilmektedir. Patlıcan, domates, biber, marul, lahana, brokoli, kereviz, karnabahar ve kırmızı pancar gibi sebze türlerinde fide ile üretim yaygın yapılmaktadır. Sebze üreticileri tohumdan, araziden ve enerjiden tasarruf sağlarken aynı zamanda homojen üretim ve erkencilik gibi avantajları sağlaması olmasından dolayı tohum yerine fide ile üretime yönelmişlerdir (Demir vd., 2010).

Günümüzde sebze tarımında kalite ve verimi artırmak için çeşitli yöntem ve teknikler geliştirilmiştir. Kullanılan bu teknik uygulamalar ile alandan tasarruf sağlamak, tohum kayıplarını azaltmak, enerjiden tasarruf sağlamak, sağlıklı ve dayanıklı bitkiler yetiştirmek ve masrafları azaltmak için yetiştiricilikte kaliteli fide kullanmak fikri benimsenmiştir. Kaliteli sebze fidesi üretiminin en önemli parametrelerinden biri olan iklim (ışık, sıcaklık ve nem) şartlarının optimum değerlerde sağlanmasıdır (Demir, 2004). Örtü altı tarımında bitki tür ve çeşitlerinin iklim istekleri doğrultusunda iklim ortamı ayarlanmalıdır. Bitkilerde temel fizyolojik olayların düzenlenmesin de ışık ve sıcaklığın etkisi en önemli çevre faktörleridir. Örtü altı tarımında çevre faktörlerinin düzenlenmesine göre bitkilerde büyüme ve gelişme periyotları kontrol altına alınmış olmaktadır (Uzun, 2001).

Bitkisel üretimde verim ve kalitenin artırılmasında etkili olabilecek rizosferden veya bazı bitkilerden izole edilen yararlı bazı farklı mikroorganizmalardan (bitki gelişimini teşvik eden rizobakteriler) yararlanılmaktadır. Biyolojik gübrelerin sürdürülebilir tarım için çok faydalı olduğu yapılan çalışmalar sonucunda saptanmıştır. Mikrobiyal türlerdeki geniş genetik varyasyon, farklı çevre koşullarına kolay adapte olabilen ve bitkisel üretim için yüksek performansa sahip mikroorganizmaların seçimi oldukça önemlidir (Çakmakçı, 2005). Yapılan bazı çalışmalarda PGPR uygulanan bitkilerde toprak üstü ve toprak altı organlarda gelişme, ürün veriminde, yaprak alanında, klorofil oranında, bitki besin içeriklerinde artış sağlandığı bildirilmiştir. Ayrıca hidrolik çalışmada, kuraklığa ve bazı hastalıklara karşı dayanıklılıkta yüksek performans sağlandığı vurgulanmıştır. PGPR'ler örtüaltı, tarla şartları ve laboratuar koşullarında uygulanabilmekte, ancak tarla denemelerinde çevre şartlarının olumsuz etkileri sonuçlar üzerinde olumsuz etkiler yapabilmektedir. Toprak şartlarına bağlı, düşük toprak nemi, düşük toprak sıcaklığı, değişik pH ortamları ve düşük besin içeriği ortamı mikroorganizma kolonizasyonuna zarar vermektedir (Şahin vd., 2004; Dobbelaere vd., 2001). Bakterilerin bitkisel üretimde verim ve kalite kriterleri üzerinde çok sayıda çalışma yapılmasına rağmen, sebzelerde kaliteli ve nitelikli fide üretimi çalışmalarında kullanımı sınırlıdır. Mevcut çalışmalarda elde edilen sonuçlara göre PGPR uygulamaları ile üretilen fidelerin daha kaliteli ve erken gelişim gösterdikleri bildirilmiştir (Vavrina 1999a, 1999b,

Kokalis-Burelleve vd., 2003). Dünyada sebze üretim potansiyeli yüksek olan ülkelerden biri Türkiye'dir. Bu potansiyeli değerlendirmenin en önemli araçlarından biri olan kaliteli fide üretimidir. Çalışmamızda farklı bakteri strainleri kullanılarak kaliteli ve sağlıklı fide üretimi hedeflenmiştir. Çalışmada kullanılan bakteri strainlerinin insan sağlığı ve çevreye, bitkisel gelişim ve kaliteye, tohum çimlenme hızı ve başarısına etkileri amacı ile kullanılmıştır.

MATERYAL ve METOD

Araştırma; Mersin ilinde 2019 yılı sonbahar yetiştirme döneminde (15.09.2019) yürütülmüştür. Bakteri strainleri Iğdır Üniversitesi Ziraat Fakültesi Bitki Korum Bölümün'den temin edilmiştir. Deneme gruplarında PGPR strainleri (SA7, SB39, YÖ19, YÖ15, YÖ41, SK72 10^7cfu/ml) kullanılmış olup, bunların bazı genel özellikleri Tablo 1'de verilmiştir.

Tablo 1. Çalışmada kullanılan bakteri strainleri ve özellikleri.

Strainler	Özellikler
SA7	*Erwiniachrysanthemi*biotype II: MIS benzerlik indeksi (%) 86, azot fiske etme özelliği kuvvetli pozitif, fosfor çözme özelliği pozitiftir. *Turgenialatifolia* bitki köklerini çevreleyen topraktan izole edilmiştir.
YÖ15	*Pseudomonasfluorescens*biotype F: MIS benzerlik indeksi (%) 63, azot fiske etme özelliği pozitif, fosfor çözme özelliği zayıf pozitiftir. *Thymusvulgaris* bitki köklerinden izole edilmiştir.
YÖ19	*Virgibacilluspantothenticus:* MIS benzerlik indeksi (%) 56,azot fiske etme ve fosfor çözme özelliği kuvvetli pozitiftir. *Thymusvulgaris* bitki köklerinden izole edilmiştir.
YÖ41	*Bacilluscereus*GC subgroup A: MIS benzerlik indeksi (%) 78, azot fiske etme özellikleri kuvvetli, fosfor çözme özellikleri kuvvetli pozitiftir. *Thymusvulgaris* bitki köklerinden izole edilmiştir.
SB39	*Bacilluspumilus*GC subgroup B: MIS benzerlik indeksi (%) 72,azot fiske etme ve fosfor çözme özellikleri pozitiftir. *Chenopodiumalbum* bitkisinin köklerini çevreleyen toprak kısmından izole edilmiştir.
SK72	*Bacillussubtilis:* MIS benzerlik indeksi (%) 70, azot fiske etme ve fosfor çözme özelliği pozitiftir. *Kochia sp*. Bitkisinin yaprak kısımlarından izole edilmiştir.

Bakteri Strainlerine Ait Süspansiyonların Hazırlanması

80 °C'de, % 30 gliserol ve sıvı besi yeri (LaurylBroth) içerisinde muhafaza edilen bakteriler nutrientagar katı besi ortamına çizgi ekim yapılmıştır. Ekim yapılan petriler 27 ^{0}C'ye ayarlı inkübatörde 48 saat inkübe edildikten sonra gelişen her bir bakteriden bir öze dolusu alınarak 250 ml nutrientbroth içeren erlenlere aktarılmıştır (Şekil 1). Bakteri ile kontamine edilen sıvı besi yerleri, bakterilerin aerobik gelişimi için 27 °C'ye ayarlı çalkalayıcıda 150 rpm'de 24 saat inkübasyona bırakılmıştır. Hazırlanan bakteriyel süspansiyonlar steril saf su ile seyreltilmiş ve spektrofotometrik ölçümle son konsantrasyon 10^7cfu ml^{-1}'ye ayarlanmıştır (Kotan vd., 2014; Turan vd., 2014).

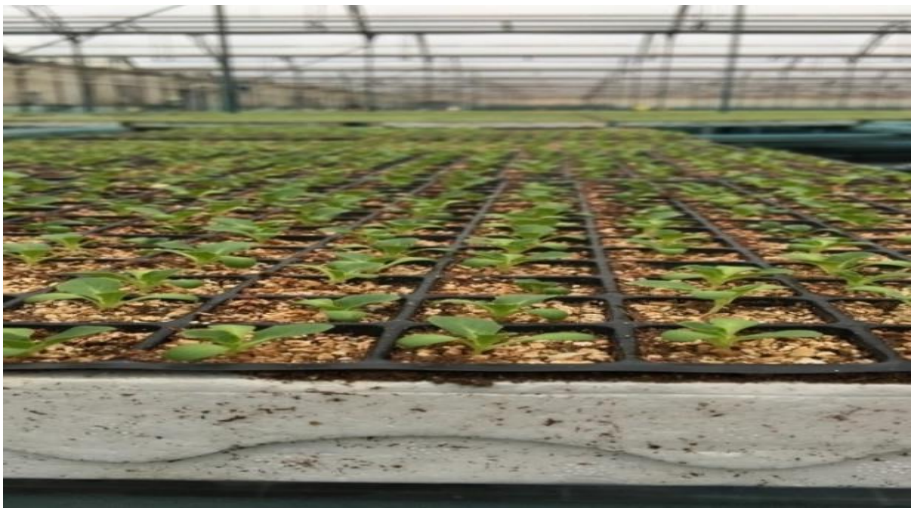
Şekil 1. Tohum bakterizasyonu işleminden genel bir görüntü.

Tohum Ekimi

Fide üretimi ticari bir fide işletmesinde (Çukurova Fide Üretim A.Ş.) gerçekleştirilmiştir. Laboratuarda kök bakterileri ile kaplanan tohumlar, fide firmasında ticari fide üretiminde kullanılan ortam (torf+perlit+vermikülit) ile doldurulan fide tepsilerine(viyol) elle ekilmiş olup (Şekil 2), daha sonra kapak atma ve sulama ticari üretime uygun tarzda gerçekleştirilmiş ve fide tepsileri çimlendirme odasına alınmıştır.

Şekil 2. Tohum ekim işleminden genel bir görüntü.

Fide üretimi ticari bir fide işletmesinde (Çukurova Fide Üretim A.Ş.) gerçekleştirilmiştir. Laboratuvarda bakterileri ile kaplanan tohumlar, fide firmasında ticari fide üretiminde kullanılan ortam (torf+perlit+vermikülit) ile doldurulan fide tepsilerine(viyol) elle ekilmiş olup daha sonra kapak atma ve sulama ticari üretime uygun tarzda gerçekleştirilmiş ve fide tepsileri çimlendirme odasına alınmıştır. Çimlendirme odasından sonra, fideler firmada organik tarım için üretilen fidelerin bulunduğu kısma alınmış (Şekil 3) ve fide üretimi sırasında bitki koruma ve bitki gelişmesini düzenleme amaçlı preparatlar uygulanmamıştır. Deneme tesadüf blokları deneme deseni düzeninde 4 tekrarlı olarak yürütülmüştür. 42 parselden oluşan denemede, her parselde 4 sıra ve her sırada 32 adet olmak üzeretoplam 5376 adet fide üretilmiştir. Usulüne uygun olarak yetiştirilen fidelerin yaklaşık 10-12 cm boyaerişip, 3-5 yapraklı oldukları dönemde (38. gün sonunda)ölçümleri yapılmıştır. Ölçümler için her parselden ortalamayı temsil eden 12 fide (Şekil 4) seçilerek ölçülmüş ve ortalamaları alınmıştır. Denemeden elde edilen veriler ANOVA varyans analizine göre "IBM SPSS statistics 23" istatistik programı kullanılarak değerlendirilmiştir. Ortalamalar arası farklılıkların karşılaştırılmasında "Duncan Çoklu Karşılaştırma Testi" kullanılmıştır.



Şekil 3. Organik tarım için üretilen fidelerin bulunduğu kısma alınan fidelerin genel görüntüsü.

Şekil 4. Araştırma sonunda elde edilen fidelerin genel görünümü.

BULGULAR ve TARTIŞMA

Tablo 2'de farklı bakteri strainleri uygulamalarının fide gelişimi ve kalitesi üzerine etkisi incelenmiştir. Araştırma sonucunda PGPR uygulamalarının fide gelişimi ve kalite özellikleri üzerine etkisi bakımından yapılan varyans analizi sonucu istatistiki açıdan anlamlı bulunmuştur. Uygulamaların bitki köksüz baş boyuna etkisi incelendiğinde; verilere göre en yüksek değer YÖ4l (8.5 cm) uygulamasından elde edilirken en düşük değer kontrol (5.4 cm) uygulamasından elde edilmiştir. Köksüz bitki boyu bakımında en yüksek değer alan YÖ41 uygulaması kontrol uygulamasına göre % 57.4 oranında artış sağlanmıştır. Uygulamaların bitki çapına etkisi incelendiğinde en yüksek değer YÖ41(5.6 cm) uygulamasından elde edilirken en düşük değer kontrol (4.1 cm) uygulamasından elde edilmiştir. Bitki çapı bakımında en yüksek değer alan YÖ41 uygulaması kontrol uygulamasına göre % 36 oranında artış sağlanmıştır. Bakteri uygulamalarının yaprak sayısına etkisinde en yüksek değer YÖ41(9adet/bitki) uygulamasından elde edilirken en düşük değer kontrol (7adet/bitki) uygulamasından elde edilmiş olup kontrol uygulamasına göre % 28.6 oranında artış sağlanmıştır. Uygulamaların yaprak enine etkisi incelendiğinde alınan en yüksek değer YÖ41 (3.9 cm) uygulamasından elde edilmiş olup en düşük değer kontrol (7 cm) uygulamasından elde edilmiştir.

Yaprak eni bakımında en yüksek değer alan YÖ41 uygulaması kontrol uygulamasına göre % 18.2 oranında artış sağlanmıştır. Uygulamaların bitki kök uzunluğuna etkisi incelendiğinde alınan en yüksek değer YÖ41 (6.8 cm) uygulamasından elde edilmiş olup en düşük değer kontrol(5.4 cm) uygulamasından elde edilmiştir. Bitki kök uzunluğu bakımında en yüksek değer alan YÖ41 uygulaması kontrol uygulamasına göre % 25.9 oranında artış sağlanmıştır (Tablo 2).

Uygulamaların bitki yaş ağırlığına etkisi incelendiğinde alınan en yüksek değer YÖ41 (4.1g) uygulamasından elde edilmiş olup en düşük değer kontrol(2,3 g) uygulamasından elde edilmiştir. Bitki yaş ağırlığında en yüksek değer YÖ41 uygulaması kontrol uygulamasına göre % 78.3 oranında artış sağlanmıştır. Uygulamaların bitki kuru ağırlığına etkisi incelendiğinde en yüksek değer olan YÖ41(1 g) uygulaması kontrol(0.6 g) uygulamasına göre % 66.6 artış sağlanmıştır. Uygulamaların bitki kök yaş ağırlığına etkisi incelendiğinde en yüksek değer alan YÖ41(1.3 g) uygulaması kontrol (0,9 g) uygulamasına göre % 44,4 oranında artış sağlanmıştır. Uygulamaların kök kuru ağırlığına etkisinde en yüksek değer alan YÖ41 uygulaması kontrol uygulamasından daha etkili olduğu anlaşılmaktadır (Tablo 3). Yapılmış olan bazı çalışmalara göre(Gagnevd.,1993; Nemecvd., 1996; Kokalis-Burellevd., 2002a, 2002b, 2003, 2006; Kloepper vd., 2004; Turan vd., 2014). PGPR'lerin sebzelerde fide yetiştiriciliğinde, fidelerde gelişim parametrelerine olumlu katı yaptığı, ürün verimi ve kalitesini artırdığı bildirilmiştir.

Tablo2. Farklı bakteri strainleri uygulamalarının fide gelişim parametrelerine etkileri.

Bakteriler	Köksüz bitki boyu(cm)*	Bitki çapı(cm)*	Yaprak sayısı (adet/bitk)*	Yaprak eni(cm)*	Kök uzunluğu(cm)*
Kontrol	5,4+-0,4c	4,1+-0,2c	7+-0,4b	3,3+-0,1c	5,4+-0,2c
SA7	7,2+-0,5b	4,9+-0,2b	8+-0,4ab	3,6+-0,1abc	6,4+-0,2ab
YÖ9	7,1+-0,3b	4,5+-0,2ab	7,8+-0,3b	3,8+-0,2ab	6,3+-0,2ab
YÖ15	6,4+-0,2b	4,4+-0,1ab	8+-0,4ab	3,5+-0,1bc	6,3+-0,2ab
YÖ41	8,5+-0,5a	5,6+-0,3a	9+-0,4a	3,9+-0,2a	6,8+-0,2a
SB36	7,4+-0,4b	4,7+-0,3ab	7,5+-0,3b	3,5+-0bc	6,1+-0,2b
SK72	6,7+-0,1b	4,6+-0,2ab	7,5+-0,3b	3,6+-0,1abc	6,3+-0,2ab
Ortalama	6,95	4,68	7,82	3,6	6,22

*Sütunlar yukarıdan aşağıya incelendiğinde aynı harfle gösterilen ortalamalar Duncan (p=0,05) testine göre istatistiksel olarak farklı değildir.

Tablo 3. Farklı bakteri strainleri uygulamalarının ağırlık olarak bazı fide gelişim parametrelerine etkileri.

Bakteriler	Bitki yaş ağırlığı(g)*	Bitki kuru ağırlığı(g)*	Kök yaş ağırlığı(g)*	Kök kuru ağırlığı(g)*
Kontrol	2,3+-0,2c	0,6+-0c	0,9+-0.1c	0,2+-0c
SA7	3,6+-0,3ab	0,8+-0,1b	1,1+-0b	0,2+-0ab
YÖ9	3,5+-0,3ab	0,8+-0,1b	1,1+-0,1b	0,2+-0b
YÖ15	3,4+-0,2b	0,8+-0,1b	1+-0.1ab	0,2+-0ab
YÖ41	4,1+-0,1a	1+-0a	1,3+-0a	0,2+-0a
SB36	3,6+-0,1ab	0,8+-0,1b	1,1+-0b	0,2+-0ab
SK72	3,6+-0ab	0,8+-0,1b	1+-0,1ab	0,2+-0b
Ortalama	3,44	0,8	1,07	0,2

*Sütunlar yukarıdan aşağıya incelendiğinde aynı harfle gösterilen ortalamalar Duncan (p=0,05) testine göre istatistiksel olarak farklı değildir.

SONUÇ ve ÖNERİLER

Çalışmada kullanılan farklı bakteri strainlerinin marulda fide gelişimi ve kalitesi üzerine etkileri değerlendirildiğinde, kontrol uygulamasına göre tüm bakterilerin fide gelişimi ve kalitesini artırdığı belirlenmiştir. Çalışmada ölçülen parametrelerde en önemli verim parametreleri olan bitki boyu, gövde yaş ağırlığı, yaprak sayısı, kök uzunluğu, bitki kuru ağırlığı ve gövde çapında önemli derecede artış olduğu belirlenmiştir. Tablo 2 ve Tablo 3'deki verilere göre, bakteri etkinlikleri incelendiğinde YÖ41 bakterisi ön plana çıkarken SA7,YÖ9, YÖ15 bakterileri sıralamayı izlemişledir. Bakterilerin bitki gelişimine ve verimine etkileri üzerine yapılan çok sayıda araştırma olmasına rağmen, sebzecilikte fide gelişimi ve kalitesi üzerine yapılmış çalışmaların yaygın olmadığı görülmektedir. Yapılan bazı araştırmalarda, PGPR uygulamaları ile fide üretiminde daha sağlıklı ve güçlü fideler yanında standart büyüklükteki fidelerin daha kısa sürede elde edildiği belirlenmiştir (Vavrina 1999a, 1999b; Kokalis-Burelle vd., 2003). Ayrıca tohuma ve fidelere yapılan PGPR uygulamalarının zararlı mikroorganizmaları kontrol altına alarak stres şartları altındaki fidelerin daha sağlıklı olmasını sağladığı belirtilmektedir (Gül vd., 2008). Marul fidelerinde uygulanan bakteri strainlerinin etkileri incelendiğinde bitkisel gelişimde ve fide çıkış sürelerinde erkencilik sağladığı, insan sağlığı ve çevreye her hangi bir zarar vermeden ekonomik olarak önemli katkılar sunduğu belirlenmiştir. Bu sonuçlara göre değerlendirme yapıldığında sağlıklı ve kalite fide üretimi için PGPR'lerin başarılı bir şekilde kullanılabileceği anlaşılmaktadır.

KAYNAKÇA

Aybak, H.Ç. (2002). *Salata/Marul Yetiştiriciliği*, Hasat Yayıncılık, 96 s. Ankara.

Çakmakçı, R., (2005). Bitki gelişimini teşvik eden rizobakterilerin tarımda kullanımı, *Atatürk Üniversitesi Ziraat Fakültesi Dergisi*, 36(1), 97-107.

Demir, İ.,Balkaya, A., Yılmaz, K., Onus, A.N., Uyanık, M., Kaycıoglu, M., &Bozkurt, B., (2010). Sebzelerde tohumluk ve fide üretimi. TMMOB-TZMO, *Türkiye Ziraat Mühendisliği VII. Teknik Kongresi,* 1, 315–346.

Demir, K.,(2004). Fide Yetiştiriciliği. *Türk-Koop Ekin Dergisi*, Aralık 6-14.

Dobbelaere, S ., Croonenborghs, A., Thy,S. A., Ptacek, D.,Vanderleyden, J., Dutto, P., & Okon, Y.,(2001). Responses of agronomically important crops to inoculation with Azospirillum. *Aust J Plant Physiol,28*, 871-879.

Eşiyok, D.,(2012). *Kışlık ve Yazlık Sebze Yetiştiriciliği*. Meta Basım, Bornova/İzmir.

Gagné, S.,Dehbi, L., Le Quéré, D., Cayer, F., Morin, J., Lemay, R., & Fournier, N. (1993). Increase of greenhouse tomato fruit yields by plant growth promoting rhizobacteria PGPR inoculated into the peat-based growing media. *Soil Biol. Biochem*, *25*, 269-272.

Gül, A.,Kıdoğlu, F., Tüzel, Y., &Tüzel, H. I. (2008).Effects of nutrition and *Bacillus amyloliquefaciens* on tomato (*Solanumlycopersicum* L.) growing in perlite. *Spanish J. Agri. Res*, *6*(3), 422-429.

Kokalis-Burelle, N.,Martinez-Ochoa, N., Rodrı´guez-Ka´bana, R., & Kloepper, J. W. (2002a). Development of multi-component transplant mixes for suppression of Meloidogyne incognita on tomato (*Lycopersicon esculentum*), *J. Nematol,34*, 362-369.

Kokalis-Burelle, N.,Vavrina, C.S., Rosskopf, E.N., & Shelby, R.A. (2002b). Field evaluation of plantgrowth-promoting rhizobacteria amended transplant mixes and soil solarization for tomato and pepper production in Florida, *Plant Soil*, *238*, 257-266.

Kokalis-Burelle, N.,Vavrina, C. S., Reddy, M. S.,& Kloepper, J. W. (2003). Amendment of musk melon and watermelon transplant media with plant growth-promoting rhizobacteria: effects on disease and nematode resistance. *Hort Technology*, *13*, 476-482.

Kokalis-Burelle, N. (2003). Effects of transplant type and soil fumigant on growth and yield of strawberry in Florida, *Plant Soil*, *256,* 273-280.

Kokalis-Burelle, N.,Kloepper, J. W., & Reddy, M. S. (2006). Plant growth promoting rhizobacteria as transplant amendment sand their effects on indigenous rhizosphere microorganisms. *Applied Soil Ecology*,*31*, 91-100.

Kloepper, J. W.,Ryu, C. M., &Zhang, S. (2004).Induced systemic resistance and promotion of plant growth by *Bacillus*spp. *Phytopathology*, *94*(11), 1259-1266.

Nemec, S.,Datnoff, L. E., & Strandberg, J. (1996). Efficacy of biocontrol agents in planting mixes to colonize plant roots and control root diseases of vegetables and citrus. *Crop Protection*, *15*, 735-742.

Uzun, S.,(2001). Serada domates ve patlıcan yetiştiriciliğinde bazı büyüme ve verim parametreleri ile sıcaklık ve ışık arasındaki ilişkiler.6. *Ulusal Seracılık Sempozyumu,* 5-7 Eylül, 97-102, Fethiye-Muğla.

Şahin, F., Çakmakçı, R., &Kantar, F.(2004). Sugar beet and barley yields in relationto inoculation with N 2-fixing an d phosphate solubilizing bacteria. *Plant and Soil*,*265*, 123-129.

Turan, M., Ekinci, M., Yildirim, E., Güneş, A., Karagöz, K., Kotan, R., & Dursun, A. (2014).Plantgrowth-promoting rhizobacteria improved growth, nutrient, and hormone content of cabbage (*Brassicaoleracea*) seedlings. *Turkish J Agri For*, *38*, 327-333.

Vavrina, C. S. (1999a).The Effect of LS213 (*Bacilluspumilis*) on plant growth promotion and systemic acquired resistance in muskmelon and watermelon transplants and subsequent field performance. *Proc Intl Symp*. Stand Establisment., p.107-111.

Vavrina, C. S. (1999b). Plant growth promoting rhizobacteria via a transplant plug delivery system in the production of drip irrigated pepper. Institute of Foodand Agricultural Sciences, *SWFREC Station Report-Veg.*, 99.6.