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More than a Vaccine. Effect of Protective Vaccines that Applicated to Geriatric Population, to the Hospitalization Profiles and Hospitalization Costs: Cross-Sectional Study

Bir Aşıdan Daha Fazlası. Geriatrik Popülasyona Uygulanan Koruyucu Aşıların Hastaneye Yatış Profillerine ve Hastanede Yatış Maliyetlerine Etkisi: Kesitsel Çalışma

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ABSTRACT Objective: Influenza and pneumococcal infections, cause life-threatening conditions in geriatric population by physiological changes and comorbid diseases. In our study, the pneumococcal/influenza vaccination status of the geriatric population hospitalized with the diagnosis of respiratory infections and their effects to the prognostic and demographic factors of the patients and the costs of hospitalization, were investigated. **Material and Methods:** Sociodemographic clinical findings and pneumococcal/influenza vaccination status of patients hospitalized with the diagnosis of non coronavirus disease-2019 respiratory tract infections between 1st January and 31th December 2022, were analyzed retrospectively. **Results:** A total of 944 patients were evaluated in our study. We determinated that 75.5% of all patients were discharged and 24.6% of patients died. It was determined that 12.3% of the patients had both pneumococcal and influenza vaccines, 9.7% were vaccinated only with influenza and 56.9% were not vaccinated with any vaccine. Pneumococcal and/or influenza protected patients were found to have significantly lower mortality rates and hospitalization costs compared to patients without vaccine protection ($p<0.001$). It was observed that single influenza vaccine protection was more effective and protective than single pneumococcal vaccine protection. **Conclusion:** Influenza vaccine addition to the routine vaccination program might significantly reduces the financial burden on the hospital/state for geriatric patients.

Keywords: Pneumococcal vaccination; hospitalization; health care cost

ÖZET Amaç: İnfluenza ve pnömokokal enfeksiyonlar, fizyolojik değişiklikler ve eşlik eden hastalıklar ile geriatrik popülasyonda yaşamı tehdit eden durumlara neden olmaktadır. Çalışmamızda, solunum yolu enfeksiyonu tanısı ile hastaneye yatırılan geriatrik popülasyonun pnömokok/influenza aşılanma durumları, hastaların prognostik ve demografik faktörlerine ve yatış maliyetlerine etkileri araştırıldı. **Gereç ve Yöntemler:** 1 Ocak-31-Aralık 2022 tarihleri arasında koronavirüs hastalığı-2019 dışı solunum yolu enfeksiyonu tanısı ile yatırılan hastaların sosyodemografik özellikleri ile klinik bulguları ve pnömokok/influenza aşılama durumları retrospektif olarak incelendi. **Bulgular:** Çalışmamızda toplam 944 hasta değerlendirildi. Tüm hastaların %75,5'inin taburcu edildiği ve %24,6'sının eks olduğu belirlendi. Hastaların %12,3'ünün hem pnömokok hem de influenza aşısı yaptırdığı, %9,7'sinin sadece influenza ile aşılandığı ve %56,9'unun ise herhangi bir aşı ile aşılanmadığı tespit edildi. Pnömokok ve/veya influenza korumalı hastaların ölüm oranlarının ve hastanede yatış maliyetlerinin aşı koruması olmayan hastalara göre anlamlı olarak düşük olduğu saptandı ($p<0,001$). Tek influenza aşısı korumasının, tek pnömokok aşısına göre daha etkili ve koruyucu olduğu görüldü. **Sonuç:** Rutin aşılama programına grip aşısının eklenmesi, geriatrik hastalar için hastane/devlet üzerindeki mali yükü önemli ölçüde azaltabilir.

Anahtar Kelimeler: Pnömokok aşısı; hastaneye yatış; sağlık bakımı maliyeti

As all around the world, the size of the geriatric population over 65 is increasing in our country too.[1] The geriatric population will exceed 12 million in 2025, and the average life expectancy will increase to 78.5 years in 2050 due to the decrease.[2] The aging and decreasing response of the immune system, in-

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creases the susceptibility to infections in advanced age and leads to a more severe course of complications due to infections.[3] According to the data of 2018, respiratory tract infections are the 3rd most common cause of mortality in the geriatric group.[4] Influenza and pneumococcal infections appear as the most responsible agents.[5-7] Pneumococcal bacteria cause the death of more than 1.5 million people annually in the World.[8] These 2 agents also bring a serious economic burden to individuals for frequent hospitalizations, long-term medical treatment, intensive care unit and mechanical ventilation.[6] For all these reasons, a periodical vaccination program against influenza and pneumococcal agents in the geriatric age group is found cost-effective.[9,10] As will be discussed in our study, it has been determined that vaccination has a very positive effect on cost reduction in a small number of studies.[11] However, we think that our study, which aims to examine the difference between the hospitalization parameters and hospitalization costs of influenza and pneumococcal vaccines in the geriatric population over 65 years of age, will make an additional contribution to the literature in this regard.

MATERIAL AND METHODS

The target population of this cross-sectional retrospective study was the patients over the age of 65 who were hospitalized for respiratory system infection in the service and intensive care units of İnegöl State Hospital between January 1 and December 31, 2022. The study was conducted in accordance with the principles of the Declaration of 2008 Helsinki. The study was approved by Bursa Yüksek İhtisas Education and Research Hospital Ethics Committee with the date 02.11.2022 and the decision number 2011-KAEK-25 2022/11-13. Demographic datas, medical records, hospitalization anamnesis and cost analyzes of the patients were filled in accordance with the data in the hospitalization file. Pneumococcal vaccine and influenza vaccine application status of individuals were examined with the Vaccine Tracking System. If they did, whether they were in the protection period (last 1 year for Influenza Vaccine, last 5 years for Pneumococcal 23 Vaccine, last 1 year for Pneumococcal 13 Vaccine) was examined and recorded. The data were evaluated according to the level of significance ($p<0.05$) using the SPSS IBM 20,0 (SPSS Inc, Chicago, IL) program.

RESULTS

In our study, geriatric patients hospitalized with the diagnosis of respiratory system infections were evaluated retrospectively. In order to purify the study results from the effects of coronavirus disease-2019 (COVID-19) infection, a total of 183 patients whose polymerase chain reaction (PCR) positivity and COVID-19 infection were confirmed or whose PCR test was negative (clinical/radiological COVID-19 infection) were excluded from the study. Based on hospitalization, being vaccinated at the appropriate dose and time was accepted as preventive prophylaxis and the vaccines administered to the cases from the system were scanned and recorded. In the examination, 44 patients with pneumococcal vaccine, 87 patients with influenza vaccine and 26 patients with both vaccines were excluded from the study because they had passed the vaccine protection period. Of the 944 patients included in our study, 440 (46.6%) were female and 504 (53.4%) were male, with a mean age of 77.9 (min 65/max 105). The mean, minimum and maximum data of the cases are given in Table 1.

It was observed that 713 (75.5%) of the patients were discharged and 231 (24.5%) patients were died. It was determined that 610 (64.6%) of the cases were treated in clinic, 250 (26.5%) in intensive care unit and 84 (8.9%) both in clinic and intensive care unit. There was concomitant disease in 875 (92.7%) of 944 cases. Of the cases, 324 (34.3%) had a diagnosis of chronic obstructive pulmonary disease (COPD). It was seen that mechanical ventilation treatment was applied in 184 (19.5%) patients. Vaccination status of the patients was categorized into four groups as shown in Table 2.

1) Both pneumococcal and influenza protection (n=116, 12.3%), 2) Pneumococcal protection only (n=198, 21.0%), 3) Influenza protection only (n=92, 9%), and 4) Not under any vaccine protection (n=538, 57.0%).

Laboratory and anamnestic datas of these four vaccination groups are shown in Table 3.

TABLE 1: Means of datas of the cases.

Means of datas	Minimum	Maximum	Means
Age (years)	65	105	77.9±7.7
Total hospitalized days	1	107	7.9±9.7
Hospitalization last 1 year with same cause	0	9	0.3±0.8
Days with antibiotic	1	53	6.2±6.2
Comorbid disease	0	6	2.0±1.1
PaO_2 (mmHg)	31	99	89.3±11.1
WBC (mcL)	770	39.760	11.036±5.5
Haemoglobin (g/dL)	5.8	18.6	12.0±2.2
Neutrophil/lymphocyte ratio	9.0	97.3	77.2±13.2
AST (IU/L)	2	2.058	45.6±11.5
ALT (IU/L)	1	2075	33.7±10.5
Glucose (mg/dL)	46	771	151.4±76.8
Urea (mg/dL)	10	362	68.2±48.4
Creatinine (mg/dL)	0.2	11.2	1.2±0.9
CRP (mg/L)	0	448	81.7±91.6
Bed costs (₺)	60	296.800	5.109.9±181.4
Medical costs (₺)	25	13.773	904.2±354.2
Other costs (₺)	206	278.867	1.260.2±933.3
Total hospitalization costs (₺)	587	532.241	9.475.5±354.8

WBC: White blood cell; AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; CRP: C-reactive protein.

TABLE 2: Distribution of the cases according to their vaccine protection status.

Vaccine group	Pneumococ	Influenza	n	%
Group 1	(+)	(+)	116	12.3
Group 2	(+)	(-)	198	21.0
Group 3	(-)	(+)	92	9.7
Group 4	(-)	(-)	538	57.0
	Total		944	100.0

TABLE 3: Laboratory and anamnestic datas of the vaccine protection groups.

Means	P (+)/I (+)	P (+)/I (-)	P (-)/I (+)	P (-)/I (-)
WBC (mcL)	10.200.5±574.2	10.900.2±894.1	10.290.3±503.2	11.258±524.2
Haemoglobin (g/dL)	11.9±2.1	12.2±2.1	12.1±2.1	11.9±5.7
Neutrophil/lymphocyte ratio	74.7±13.8	76.3±13.3	74.5±14.2	78.3±12.7
AST (IU/L)	30.2±21.9	36.5±5.9	35.3±7.8	51.6±13.7
ALT (IU/L)	23.4±18.8	32.3±12.2	30.5±8.9	33.6±8.9
Glucose (mg/dL)	146.7±66.1	149.5±80.6	147.9±71.8	152.9±74.3
Urea (mg/dL)	66.9±49.7	63.9±43.7	68.1±54.6	70.5±48.6
Creatinine (mg/dL)	1.2±0.8	1.2±0.8	1.2±0.9	1.2±0.9
CRP (mg/L)	71.1±8.9	74.6±9.2	69.7±8.5	88.1±9.2
Topal hospitalization days	3.6±3.5	6.2±4.2	4.1±4.1	9.5±1.1
Bed costs (₺)	386.1±22.7	2.387.4±56.8	519.5±104.2	4.450.±2
Medical costs (₺)	336.0±66.8	711.9±113.1	451.7±104.2	1069.2±120.9
Imaging costs (₺)	123.8±97.2	132.9±73.5	144.9±113.6	198.2±117.1
Laboratory costs (₺)	43.7±11.3	54.5±19.1	127.2±18.2	135.4±22.2
Total hospitalization costs (₺)	1.037.1±358.4	3.788.8±321.7	1.277.9±388.6	14.144.9±618.3
PAO_2 (mmHg)	92.0±8.9	89.8±11.1	91.9±8.5	89.3±1.1
Days with antibiotic	3.5±1.2	8.1±3.0	6.3±2.8	9.8±3.1

WBC: White blood cell; AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; CRP: C-reactive protein.

It was observed that the rate of pneumococcal vaccine protection in men was higher than in women. Similarly, 134 of 324 patients diagnosed with COPD were found to be under pneumococcal vaccine protection. This rate was found to be higher when compared to 29.0%, corresponding to 180 of 620 patients without COPD diagnosis. It was observed that patients vaccination due to hospitalized less frequently in intensive care units, mechanical ventilator requirement and died. Total hospitalization costs were less when compared with the patients not receiving any vaccination protection. İnfluenza vaccine protection was higher. In addition, the number of antibiotic days, total hospitalization days, costs of hospitalization were found to be lower in influenza vaccine protection (Table 4).

Difference between the two groups in terms of death status, the number of hospitalizations with the same diagnosis in the last year, the rate of mechanical ventilation requirement and the rate of intensive care unit admission were not detected (Table 5).

In the correlation analyzes, the total hospitalization costs were correlated significantly with ages, total hospitalization days, white blood cell count, neutrophile/lymphocyte ratio, glucose levels positively; with $PaSO_2$ levels at hospitalization and haemoglobin levels negatively. The numbers of concomitant diseases and the total hospitalization costs were positively correlated, but it was not statistically significant.

DISCUSSION

The geriatric population, whose rate is increasing gradually in the society, is accompanied by immunosenescece which is the natural process of old age and chronic diseases.[3] This condition creates a basis for vaccine-preventable respiratory tract infections with high mortality and morbidity.[12] Influenza and pneumococcal infections appear as the most detected agents in this category.[13] It has been reported that more than 90% of influenza and pneumococcal deaths occur in the geriatric group.[14] In our study, it was determined that the influenza group only, the

TABLE 4: The comparison of anamnestic datas of pneumococ and influenza groups.

	P (+)	I (+)	p values
Days with antibiotic	6.33±5.3	3.61±2.9	*p<0.001*
Total hospitalization days	7.74±0.6	4.80±0.4	*p<0.001*
Bed costs (₺)	3.549.73±663.4	686.19±290.3	*p<0.001*
Total hospitalization costs (₺)	5.400.87±690.8	1.581.75±423.7	*p<0.001*
Medical costs (₺)	930.18±23.2	596.39±13.6	*p<0.001*
Need intensive care	n=64 (32.3%)	n=11 (12.0%)	*p<0.001*
Need mechanical ventilation	n=37 (16.7%)	n=5 (5.4%)	*p=0.008*
Ex status	n=46 (23.2%)	n=8 (8.7%)	*p=0.003*

TABLE 5: Comparison of datas of groups with both vaccine protection and influenza protection only.

	P (+) ve I (+)	P (-) ve I (+)	p values
Days with antibiotic	3.5±1.2	6.3±2.8	p=0.002
Total hospitalization days	3.6±3.5	4.1±4.1	p=0.001
Bed costs (₺)	386.1±22.7	519.5±104.2	p<0.001
Medical costs (₺)	336.0±66.8	451.7±104.2	p<0.001
Imaging costs (₺)	123.8±97.2	114.9±113.6	p=0.017
Laboratory costs (₺)	43.7±11.3	127.2±18.2	p=0.002
Total hospitalization costs (₺)	1.037.1±358.4	1277.9±388.6	p<0.001
Need intensive care	n=19 (16.3%)	n=11 (12.0%)	p=0.437
Hospitalization in 1 year with same cause	n=21 (18.1%)	n=19 (20.7%)	p=0.724
Need mechanical ventilation	n=5 (4.3%)	n=5 (5.4%)	p=0.759
Ex status	n=10 (8.6%)	n=8 (8.7%)	p=1.000

pneumococcal group only, and the group protected by both vaccines were hospitalized less, lower intensive care unit submission and the mechanical ventilation requirement. In a meta-analysis, it was shown that influenza vaccine reduced deaths by 39-68%, hospitalizations by 50-61%.[15] In another study, it was found that the vaccine reduced the rate of hospitalization in the intensive care unit (82%) and the mortality rate (80%).[16] Similarly, in studies evaluating the efficacy of pneumococcal vaccine reduced hospitalizations due to pneumonia (45%) and the risk of death (59%).[17] In the study of Chan Carusone et al., it was observed that pneumococcal vaccine showed a negative relationship with hospitalization.[18] In our study, it was defined that those who are only under influenza vaccine protection, were hospitalized less frequently in clinic or in intensive care unit, mechanical ventilation requirement and were less died compared. The influenza vaccine is more advantageous than the pneumococcal vaccine. This result of our study, which gives the chance to compare two different vaccines in terms of hospitalization parameters and hospitalization costs, will make an additional contribution to the literature. Another result we reached in our study is on the relationship between vaccine and sex. In our study, pneumococcal vaccine was found to be significantly higher in males but a similar relationship was not seen for influenza vaccine. In the study of Vural et al., it was shown that influenza vaccination frequency did not differ between women (39.1%) and men (38.0%), in line with our data. However, when the pneumococcal vaccine was compared in terms of gender, no difference was found between women (8.1%) and men (8.0%), which is different from the data of our study.[19] The data that we found in our study that the pneumococcal vaccination rate in patients with COPD was significantly higher than in patients without it, supports the similar data obtained in Bülbül et al. study.[20] In the study of Aka Aktürk et al. that pneumococcal vaccine application was found to be high in patients with COPD, although it was not statistically significant.[21] In the same study, it was reported that the frequency of influenza vaccine administration was significantly higher in patients with COPD. This result differs from the data of the lack of significant difference in our study.[21] İnal et al. also showed in their study that the positive relationship between total hospitalization costs and total hospitalization days we reached in our study was similar.[22] Over the age of 65, pneumococcal and influenza vaccination programs make another positive contribution as well as in terms of Public Health besides to the medical conditions of the individuals. Influenza and pneumococcal infections, which can be prevented or at least their complications can be reduced by vaccination, impose a serious burden on the health economy with all kinds of medical needs they create.[23] For this reason, the opinion that vaccination is the easiest, cheapest and most strategic method to protect the health of people over 65.[5] In our study, it was determined that the influenza group had a great advantage in terms of costeffectiveness with fewer antibiotic days; less medical costs, bed costs and total hospitalization costs when compared with to the pneumococcal group. It was determined that the total hospitalization costs of the patients showed a significant correlation with the parameters that predicted severe infections and complications. In our study, the vaccination/cost relationship was analyzed in detail. There are studies showing that influenza and pneumococcal vaccines reduce the cost in the geriatric population over 65 years of age.[1,6,13,24-26] These data support our study that the both vaccines significantly reduces hospitalization costs compared to unvaccinated ones. In our study, it was determined that the groups with both vaccines were hospitalized less often and for a shorter period, were less admitted to the intensive care unit, were less mechanical ventilation requirement, were less died, and had lower total hospitalization costs compared to the group with only pneumococcal protection. Seki's study also showed that the combined application of the two vaccines is more effective in terms of medicine and cost-effectiveness compared to the single application.[27] However, unlike this study, it was shown that people who vaccinated with both vaccines used less antibiotics, had less hospitalized, had less bed/medical/laboratory/imaging costs and total hospitalization costs, compared to those who received only influenza vaccine in our study. It is an interesting data that no significant difference was found in terms of the number of hospitalizations with the same diagnosis in the last

1 year, the rates of admission to the intensive care unit, the rates of mechanical ventilation requirement and the rates of death.

CONCLUSION

It is the most rational approach to vaccinate the geriatric population over 65 years of age with pneumococcal and influenza vaccines to protect them from complications of infections with severe mortality and morbidity. Regular vaccination with both vaccines significantly reduces hospitalizations and the need for aggressive treatment. At the same time, it provides extremely significant savings on health economics. The geriatric group should be vaccinated with both vaccines for the most efficient and cost-effective protection.

Source of Finance

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Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: *Hayrettin Göçmen;* ***Design:*** *Hayrettin Göçmen, Gülçin Bölük;* ***Control/Supervision:*** *Hayrettin Göçmen, Gizem Arslan;* ***Data Collection and/or Processing:*** *Hayrettin Göçmen, Gülçin Bölük;* ***Analysis and/or Interpretation:*** *Hayrettin Göçmen;* ***Literature Review:*** *Hayrettin Göçmen, Gülçin Bölük, Gizem Arslan;* ***Writing the Article:*** *Hayrettin Göçmen;* ***Critical Review:*** *Hayrettin Göçmen, Gülçin Bölük;* ***References and Fundings:*** *Hayrettin Göçmen, Gizem Arslan.*

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