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Research Article

Polypharmacy: As a Predictive Indicator of Mortality and Length of Stay for Geriatric Patients Charged in ICU

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Abstract

Objectives: In this study, we aimed at evaluating the effect of polypharmacy on the mortality and the length of stay of elderly patients that charged in the ICU.

Methods: The patients aged 65 and over which were admitted to the intensive care unit between the dates of September 2018 and August 2019 were included in this study. The statistical calculations were made with SPSS and then the significant parameters were investigated seperately.

Results: In ICU, retrospectively, a positive statistical significance was found between polypharmacy and the lenght of stay with mortality rates in our study with 235 geriatric patients ($p<0.05$). When biochemical parameters were compared between polypharmacy and non-polypharmacy groups, a significant difference was found in RDW, vitamin B12, uric acid, Fe and ferritin parameters ($p<0.05$).

Conclusion: If we could make comprehensive geriatric assessments in time, we would be able to make the right diagnosis and the right choices of medication for older people and as a result we would be able to decrease the proportion of negative effects of polypharmacy to some extent.

Keywords: Aged, intensive care units, polypharmacy

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As the elderly population increases both in number and proportion, the number of geriatric patients admitted to ICU rises day by day.[1,2] US Census Bureau predicts that the number of the elderly who are aged 85 and above in the society will reach up to 19 million by 2050.[3] The current data show us that with the increase in the number and rate of the elderly, the prevalence of chronic diseases and the accompanying loss of function will also be in higher proportions as well.[4]

There are some studies examining the factors affecting the mortality and the length of stay of older people in ICU. In the study conducted by Karaveli et al.[5] in 2015, the most common six chronic diseases were determined as hypertension, coronary artery disease, hyperlipidemia, congestive heart disease, diabetes mellitus and chronic obstructive pulmonary diseases. The length of stay has been shown to be prolonged in patients with cardiovascular diseases, multiple diseases, nervous system diseases and cerebrovascular diseases.[6] In the same study, it was found that the duration of hospitalization was extended as the laboratory parameters such as urea, creatinine and sodium levels were increased. In patients with critical condition, it is insufficient to determine long-term survival and the quality of life based on age alone.[4] However, advanced age, especially after 85 years, has been shown to be associated with an increase in ICU mortality rates.[7] In another

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study, it was observed that the mortality rates were higher in the sudden and unplanned hospitalizations than in the planned hospitalizations. In the same study, it was determined that "renal functions" were effective in survival for the long-term intensive care hospitalizations, and "the severity of disease" for the short term.[8]

Polypharmacy (PFC) is a term that has not yet been agreed upon by definition, which is accepted as the use of more than one drug. Different definitions are found according to the number of drugs used in the available resources and the duration of drug use. Some sources define PFC as drug use of 4 and above, while others define drug use of 5 and above.[9–11] In some studies, 45% of hospitalized elderly patients were shown to be discharged with at least five or more drugs that were prescribed with.[12,13] Furthermore, the awareness of PFC should be planned in educational activities with covering both patients and caregivers as well as healthcare workers, as the majority of the elderly (90%) are using at least one inappropriate drug, half of which is not fully cleared, and 5-10% of the drugs they take are written for the same indication.[14,15]

Drug-drug interactions are more common in the presence of PFC and affect the clinical results to a certain extent, especially with patients charged in ICU.[16] As a result of a systematic review and meta-analysis, a relationship was found between death and PFC, but the causality relationship could not be elucidated.[17] PFC was showed in the majority of elderly patients before admission to the ICU by the studies and it is known that PFC increases the risk of developing delirium and as a result that cause an increase in mortality and morbidity.[18,19] We can reduce the risk of delirium occurrence in critical patients by changing certain medications.[20] In a community-based cohort study, it was concluded that PFC is an indicator of mortality for the elderly who use 10 or more drugs.[21]

It has been noticed that there are not too many studies in medical bibliography, which investigating the effect of PFC on mortality and length of stay in geriatric patients who charged in ICU. In this study, we aimed at revealing the effect of PFC on mortality and length of stay in patients in the internal medicine intensive care unit.

Methods

The demographic and laboratory findings of patients aged 65 and over who were charged in the ICU of our hospital between 1 September 2018 and 31 August 2019 were collected by scanning through the Probel patient registration system and analyzed by SPSS. A total of 235 patients (131 women and 104 men) with both PFC group (n=118) and non-polypharmacy (NPFC) group (n=117) were included in the study. Patients using drugs at least 4 or more were enrolled in the PFC group while patients those using less than 4 drugs were enrolled in the NPFC group. Biochemical parameters, prognostic scores, CRP and the length of hospital stay were calculated with t-test and Mann-Whitney U test. For mortality rates between groups, Pearson's chi-square test was used. Ethical approval for this study was obtained.

Results

When biochemical parameters were compared between PFC and NPFC groups, a significant difference was found in RDW, vitamin B12, uric acid, Fe and ferritin parameters. While RDW was 16.4±3.5% in the PFC group, RDW was found to be 18.6±4.4% in the NPFC group, which was statistically significant ($p<0.05$). When the two groups were compared in terms of PFC, parameters with Vitamin B12, uric acid, Fe and ferritin parameters, a statistically significant negative correlation was observed ($p<0.05$), (Table 1). CRP values were found statistically significantly lower in the PFC group (103.7±51.2 mg/l) compared to the NPFC group (121.9±70.1 mg/l) ($p<0.05$). While there was no significant difference in SOFA and APACHE II scores in both group comparisons, the length of hospital stay was found to be statistically significant and it was higher in the PFC group (9.4±8.0 days) compared to the NPFC group (6.7±6.9 days) ($p<0.05$), (Table 2). There was a statistically significant difference in mortality parameter between PFC and NPFC groups as follows: Mortality rate in the PFC group with 44.1% was significantly higher than the NPFC group with 27.4% ($p<0.05$), (Table 3).

Discussion

It has been shown that the PFC during ICU stay is significantly high in adult patients and even the number of drugs used in older people is on average of 12 different types in a study.[22] It has been determined that up to 30% of patient admissions are due to drug-related side effects or drug-induced events.[23] Multiple chronic diseases such as hypertension, chronic obstructive pulmonary disease, thyroid diseases, arthritis, heart disease, cancer and diabetes mellitus etc. cause multiple drug use in the geriatric age group. Elderly people are more sensitive to adverse events and side effects of drugs which are common due to reasons during aging process such as physiological or pathological changes, different pharmacodynamic and pharmacokinetic features or comorbidities associated with old age.[24] Prescribing cascade is used to express the condition of writing new drugs that occur as a result of misinterpretation of symptoms and findings due to the side effects or adverse events of a drug given to the patient, and it manifests itself

Table 1. Compare of biochemistry parameters between groups

Parameters	No (n=117)	Yes (n=118)	p
WBC	10.9±6.6	10.3±6.2	NS
HCT	31.4±6.2	31.3±5.7	NS
HGB	10.1±1.0	10.2±1.1	NS
NEU	8.4±5.1	8.5±5.6	NS
LYM	1.8±3.1	1.5±2.2	NS
PDW	15.6±13.9	14.3±3.0	NS
RDW	16.4±3.5	18.6±4.4	p<0.05
PLT	191.4±142.1	203.3±130.6	NS
MPV	13.4±25.8	12.6±14.6	NS
HbA1c	7.1±6.0	6.5±1.5	NS
Urea	101.5±65.2	99.7±75.5	NS
Creatinine	7.7±33.5	7.4±41.8	NS
AST	75.9±210.6	51.8±100.0	NS
ALT	46.5±93.5	37.5±79.2	NS
Sedimentation	61.3±26.1	58.7±28.5	NS
Albumin	2.6±0.6	3.0±3.0	NS
Total Bilurubin	2.4±4.4	1.8±3.5	NS
Parathyroid hormone	117.2±123.7	134.2±140.6	NS
Cortisol	33.5±21.5	30.1±15.4	NS
Ca	8.4±1.0	8.2±0.9	NS
P	4.1±3.2	3.5±1.4	NS
Vitamin D	18.5±13.2	17.2±13.5	NS
Vitamin B12	625.3±461.2	459.6±362.7	p<0.05
Uric asid	7.9±4.9	6.5±3.3	p<0.05
Fe	63.6±66.9	46.4±42.4	p<0.05
Ferritin	546.0±553.8	472.4±1049.4	p<0.05

WBC: White blood cell; HCT: Hematocrit; HGB: Hemoglobin; NEU: Neutrophils; LYM: Lymphocytes; PDW: Platelet distribution width; RDW: Red cell distribution; PLT: Platelet; MPV: Mean platelet volume; AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; Ca: Calcium P: Phosphorus NS: Not significant, p<0.05 was considered significant. t-test and Mann-Whitney U test were used.

Table 2. Compare of inflamation and systems of score parameters between groups

Parameters	No (n=117)	Yes (n=118)	p
CRP	121.9±70.1	103.7±51.2	p<0.05
SOFA score	10.6±2.5	10.0±2.8	NS
APACHE II score	22.7±4.3	22.1±4.3	NS
Time of stay	6.7±6.9	9.4±8.0	p<0.05

CRP: C-reactive protein; SOFA: Sequential organ failure assessment; APACHE: Acute physiology and chronic health evaluation; NS: Not significant, p<0.05 was considered significant. t-test and Mann-Whitney U test were used. Patients using immunosuppressive drugs were excluded from the study.

Table 3. Mortality rates in patients with polypharmacy

	Mortalite		
	Ex	Live	Total
Polypharmasic			
Yes			
Count	52	66	118
Expected count	42.2	75.8	118.0
% within polypharmasic	44.1%	55.9%	100.0%
% within mortality	61.9%	43.7%	50.2%
No			
Count	32	85	117
Expected count	41.8	75.2	117.0
% within polypharmasic	27.4%	72.6%	100.0%
% within mortality	38.1%	56.3%	49.8%
Total			
Count	84	151	235
Expected count	84.0	151.0	235.0
% within polypharmasic	35.7%	64.3%	100.0%
% within mortality	100.0%	100.0%	100.0%

Pearson's chi-square test was used. p<0.05 was considered significant. (χ^2=7.149, p=0.008).

in different occasions and level of severity with many different stages.[25] The atypical course of geriatric syndromes with multiple comorbidity, especially in the elderly, causes multiple drug use and may result in the development of prescribing cascade.

In a community-based cohort study involving 601 elderly participants in Finland, which the total mortality rates in the PFC group were analyzed in 3 groups in 2 different time periods, it has been found that the mortality rates were 55% and 61% of those who use 10 or more drugs, 33% and 40% of those who use drugs between the numbers of 6 and 10, and finally 27% and 23% in the NPFC group.[21] The mortality rates was saved in papers with the follow-up of the participants by calculating the death records in Finland and it is thought-provoking that there is a statistically significant positive relationship between mortality and PFC rates (p<0.001). In our study with elderly people in ICU, the mortality rate was 44.1% in the PFC (4 or more drug users) group and 27.4% in the NPFC (less than 4 drugs) group, which can be said to be compatible with each other (p<0.05). Furthermore, the mortality rates were almost similar to our study other than patients used 10 and more drugs in which was found to be a higher rates of mortality compared to rest of the groups in Finnish study as well as our PFC group in study. But the Finnish study does not give physicians any information about the association between PFC and the length of stay among elderly people charged in ICU.

Moitra et al.[26] demonstrated in a retrospective study with 34.696 subjects that the mean length of stay of ICU in geriatric patients was 3.4 days (±4.5 d) and they found that

long-term mortality rates increased with the length of stay of ICU, but there was not any information which compares PFC with the length of stay and mortality rates. In a study with 1335 elderly people in internal medicine wards, Nobili et al.[27] found that PFC was not related to the length of hospital stay or in-hospital mortality, but adverse events were strongly related to the risk of prolonging hospital stay or in-hospital mortality and with every one of the adverse event the length of stay prolonged by 3.57 days ($p<0.0001$). But this study involved just patients charged in wards, not in ICU. We revealed that the lenght of stay was was found to be statistically significantly higher in the PFC group (9.4±8.0 days) compared to the NPFC group (6.7±6.9 days) in our study which was done in ICU ($p<0.05$). In a review study, the education of healthcare providers, particularly by clinical pharmacists, is a vital part of a strategy to prevent medication errors can lead a great reductions in the mortality rate, drug costs, and length of stay.[28] So for those reasons that we mentioned above, there should be awareness studies of PFC and its effects on human health for both healtcare providers and patients, since it would decrease the PFC rates to some extent among patients.

Conclusion

With this study, we revealed that the mortality rates and the prolonged length of stay increased in geriatric patients with PFC that charged in ICU. We agree with the opinion that the PFC can be used as a predictive indicator of the mortality and length of stay.

Disclosures

Ethics Committee Approval: The study was approved by SBU Bozyaka Research and Training Hospital (date: 11.03.2020, number: 01).

Peer-review: Externally peer-reviewed.

Conflict of Interest: The authors have no conflicts of interest to report.

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