Benefits of Pharmacist Intervention in the Critical Care Geriatric Patients with Infectious Diseases: A Propensity Score Matching Retrospective Cohort Study

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Abstract

Background

The variabilities of the pharmacotherapeutics' efficacy and safety in the ICU geriatric patients further highlighted the importance of optimization of antimicrobial therapy. The aim of our study was to assess the impacts of clinical pharmacist intervention on antibiotic use, cost outcomes, and clinical benefits of the geriatric patients with infectious diseases in the critical care unit (ICU).

Methods

A propensity score matching (PSM) retrospective cohort study was undertaken in ICU patients with infectious diseases from 2017 to 2019. Baseline demographic, pharmacists' activities and clinical outcomes including the patients' mortality, antibiotic utilization, length of ICU stay (LOS), and costs of the drugs were compared between these two groups. Univariate analysis and bivariate logistic regression were adopted to illustrate the influencing factors on the mortality outcome.

Results

Of 1523 patients evaluated during the observed period, a total of 102 geriatric ICU patients with infectious diseases were enrolled in each group after PSM matching. Top 5 recommendations occurred by the pharmacist were medication regimen adjustments by diseases on progression, medication regimen adjustments by microbial results, drug withdrawal by full treatment courses, suggestions for TDM and medication regimen adjustments by de-escalation. The antibiotic use density (AUD) of all antibiotics consumed decreased significantly ($p=0.018$) from 241.91 DDD/100 bed days in the control group to 176.64 DDD/100 bed days in the pharmacist exposed group. AUD proportion was dropped in carbapenems from 23.07% to 14.43% and tetracyclines from 11.56% to 6.26% after pharmacist interventions. Although the mortality or LOS had no statistical difference between these two groups, the total cost of antibiotics was reduced significantly from \$836.3 (IQR 426.88, 1682.09) in the control group to \$362.15 (IQR 148.23, 1034.4) ($p<0.001$) in the pharmacist intervention group, and cost for all the medications were reduced from \$2868.18 (\$1268.44, \$5059.00) to \$1941.5 (\$1092.89, \$3538.97) ($p=0.016$). Univariate analyses showed that there was no statistically difference in pharmacist intervention between the groups of survival and death ($p=0.288$).

Conclusions

The services provided by the critical care pharmacist could promote the rational use of drugs, which benefit both ICU geriatric patient and hospital care.

1. Introduction

As infections occur most frequently among the geriatric patients in the intensive care unit (ICU), antibiotics become the most commonly prescribed drugs in the ICU [1, 2]. Compare to the general wards, ICU often has to manage the challenges of co-administration of multiple intravenous medicines, limited physiological reserve, hemodynamic instability, and a variety of complications related to prolonged immobilization and recumbent positioning as well as changes in parameters of pharmacokinetics and pharmacodynamics (PK/PD) of

administrated drugs [3, 4]. All these increased variabilities of the pharmaco-therapeutics' efficacy and safety in the ICU patients further highlighted the importance of optimization of antimicrobial therapy including optimal drug dose, frequency, delivery route, duration of antibiotics, or drug adverse reaction (ADR) occurrence rates of the antibiotics, that are completely different from those in the general ward [4]. Understanding these challenges at ICU is critical for the best practice of antibiotic prescription for both physicians and pharmacists for optimal antibiotic therapy.

In recent years especially during COVID 19 pandemic, clinical pharmacists are gaining more and more attention worldwide as critical members of the ICU patient care team to achieve optimal use of medications and optimal patient outcome. Several studies pointed out the positive impact of clinical pharmacists on the health care of patients with chronic diseases such as cardiovascular diseases, atrial fibrillation, diabetes and so on [5–7]. Care of critical geriatric patients has become a multidiscipline [8]. Antimicrobial stewardship (AMS) programs have been developed for optimizing the regimens of infections and reducing infection-related morbidity and mortality [9, 10]. The critical care pharmacist in the ICU group could identify prescription errors, monitor, or adjust the dosage and identify adverse effects related to the co-administration of multiple medicines, optimize antibiotics adoptions [11], as well as improve the clinical and economic outcomes [8, 12–14].

In China, pharmacist intervention in ICU patients care is still under developing stage [15]. Currently, the training cycle of clinical pharmacists who are competent for their posts is too long to assign one clinical pharmacist to each ICU in the large medical institutions and the benefit of critical care pharmacists was also not fully demonstrated in the ICU. So in this study, we objected to highlight the valuable contributions of clinical pharmacy services in critically ill patients. We aimed at evaluating the effectiveness and economic affections of the clinical ICU pharmacist on critical the geriatric infectious patients.

2. Methods

2.1 Study Design and setting

The study was performed in an 1100-bed academic university-affiliated tertiary-care hospital in China: Beijing Shijitan Hospital with a 20-bed medical-surgical ICU. This was a single-center, retrospective, cohort study. The study was divided into two groups: a group without pharmacist intervention as the control group from January 1, 2017, to December 31, 2017, and a group with pharmacist intervention as the pharmacist-exposed group from January 1, 2019, to December 31, 2019. Ages of all the patients were ≥ 65 years old.

Patients were excluded if 1) their inpatient department or admission department were not ICU; 2) missing information about documented discharges; 3) not using antibiotics in the ICU; 4) have extreme outliers with laboratory tests such as glutamic pyruvic transaminase (ALT) or glutamic oxaloacetic transaminase (AST) >1000 and length of ICU stay (LOS) ≤ 1 or ≥ 30 days.

2.2 Pharmacist Practice

The clinical pharmacist, with more than 10 years of hospital practice experience, was assigned to the ICU ward to guarantee the continuity and quality of the interventions. The pharmacist has a major in anti-infectious

diseases and completed all the rotational training including 5 years of pharmacist resident training and 1 year of infectious disease specialty residency.

During the observed period, the ICU pharmacist attended daily unit rounds with ICU physicians at least 20 hours a week. Based on the professional guidelines or standards, the pharmacist focused on optimization of anti-infectious pharmacotherapy such as indication, usage and dosage, curative effect, adverse drug reaction (ADR), and treatment course, to assure the rationalities of the patients' anti-infectious therapy. The pharmacist-identified medication-related errors would then be shared and fully discussed with the senior physicians. The optimized prescription would not be performed until the pharmacist and senior physicians formed consensus ideas. Pharmacist consultative services on the general pharmaceutical information, or interpretations of pharmacokinetic parameters were also available as part of daily work in the ICU ward.

2.3 Covariates

Antimicrobial use and the covariates were collected for all patients admitted to the ICUs during the study periods. Age, gender, and race were collected as baseline demographics. The CCI, APECH-II score, white blood cell (WBC), neutrophil percentage (NE%), C-reactive protein (CRP), procalcitonin (PCT) and diagnoses of infections with ICD 10 code within 48 hours of patient admission was extracted as the baseline clinical characteristics. Pharmaceutical service information was obtained from the ICU pharmacist's daily records. The rate of consensus was defined as the percentage of recommendations agreed upon by the ICU physicians and the ICU pharmacist during the exposure period.

2.4 Outcomes and measurement

The primary outcome parameters were hospital mortality during the ICU hospitalization. The secondary outcome parameters were antibiotic use density (AUD) proportion and AUD descender (%), LOS, antibiotic charges and total drug charges. Routine antibiotic uses in ICU including carbapenems (Meropenem, Imipenem and Cilastatin Sodium), broad-spectrum penicillin (Piperacillin Sodium And Tazobactam Sodium), third-generation cephalosporins, monocyclic lactams (Ceftazidime, and cefoperazone Sodium And Sulbactam Sodium), fluoroquinolones, aminoglycosides, tetracyclines (Minocycline and Tigecycline), glycopeptides and oxazolidinone and systemic antifungal agents. The ATC classifications (Anatomical Therapeutic Chemical classification) of antibiotics were referenced by the World Health Organization (WHO) [16].

For the use of the antibiotic, the defined daily doses (DDD), number of occupied bed days, and the antibiotic use density (AUD) were adopted. The standard DDD of antibiotics was confirmed on the website of WHO [17]. The density of antibiotic use DDD/100 bed days (AUD) ^[18] as one of the antimicrobial drug management indicators in China was calculated. The methodology was supported by World Health Organization ^[19]. And then the influence of ICU clinicians' prescription tendency of certain kinds of antibiotics were measured by the AUD proportion or AUD descender. The calculation formulas were as followings:

$$AUD = \frac{(\text{Accumulative drug consumption (g)/DDD})}{\text{Number of occupied bed days (Day)}} \times 100$$

$$AUD \text{ proportion (\%)} = \frac{AUD \text{ of certain kinds of antibiotics before or after pharmacist attendance}}{\text{Total AUD of all the kinds of antibiotics before or after pharmacist attendance}} \times 100\%$$

$$AUD \text{ descender (\%)} = \frac{AUD \text{ before pharmacist attendance} - AUD \text{ after pharmacist attendance}}{AUD \text{ before pharmacist attendance}} \times 100\%$$

2.5 Statistical analysis

We used 1:1 propensity score matching (PSM) to control for potential confounders, which were measured age, baseline Acute Physiology and Chronic Health Evaluation II (APECH-II) score, procalcitonin (PCT), and Charlson comorbidity index (CCI). Propensity score matching (PSM) was adopted as a 1:1 ratio between the pharmacist-exposed and the control group. The caliper was set as 0.25.

Descriptive statistics were used to characterize the study group. Normally distributed data, non-normal distribution continuous data, and categorical data were presented as mean $\pm$ standard deviation, medians (interquartile range, IQR) and number (frequency), respectively. Data recorded were compared using the Pearson chi-square test or the Fisher exact test for categorical variables or the Student's t-test or the Mann-Whitney U test for quantitative variables according to the conditions of application. Univariate analysis and bivariate logistic regression were adopted to illustrate the influencing factors on the mortality outcome.

The main infectious diseases diagnosed in this study population were also described and the corresponding ICD-10 code was shown. The costs of antibiotics or the total agents were also collected as one economic indicator and the exchange rate between the RMB and the US dollar was subject by the State Administration of Foreign Exchange in China. The exchange rate on May 11, 2021, was US 100\$ = RMB 643.61yuan.

All data were analyzed using SPSS version 25.0 (SPSS Inc. Chicago, Illinois, USA). All significance tests were two-tailed, and $p < 0.05$ was considered statistically significant.

3. Results

3.1 Demographic characteristics

A total of 561 cases were included in the initial analysis, with 270 in the control group and 291 in the pharmacist-exposed group. A comparison of baseline characteristics between control group and pharmacist-exposed group before and after propensity score matching is shown in figure 1 and table 1, which also showed a brief overview of the main infectious diseases type diagnosed. Basic demographic characteristics in both groups are similar to each other after PSM matching including the age, gender, race and baselines of APECH-II score, CCI score and results of lab examinations. After PSM, The median age of the patients encompassed in this study was 85 years old in the control group and 84 years in the pharmacist-exposed group. The ratio of men and women is close to 1:1 in both two groups. The median values of baseline APECH-II score was 24 in the control group and 22 in the pharmacist-exposed group. The median values of baseline CCI was the same

between the two groups which was 5. We also found bacterial pneumonia (29.85%), sepsis (23.79%), urinary infection (13.59%), and septic shock (11.17%) were the main infectious diseases diagnosed during the study period, and then were the fungal pneumonia (5.83%) and fungal urinary infection (1.84%). There is no significant differences of infectious diseases types between control group and the pharmacist intervention group.

Tab 1

Baseline Characteristics of study patients before and after PSM

	Before PSM			After PSM		
	The control group N=270	The pharmacist-exposed group N=291	p	The control group N=102	The pharmacist-exposed group N=102	p
Age (Median year, IQR)	85.50 (79.00, 90.00)	83.00 (74.00, 88.00)	0.002*	85.00 (77.00, 89.00)	84.00 (74.00, 89.00)	0.716
65~84y, n (%)	96.00 (35.56%)	144.00 (49.48%)		36.00 (35.29%)	49.00 (48.04%)	
≥85y, n (%)	146.00 (54.07%)	121.00 (41.58%)		54.00 (52.94%)	46.00 (45.10%)	
Gender, male, n (%)	149.00 (55.19%)	148.00 (50.86%)	0.305	47.00 (46.08%)	49.00 (48.04%)	0.780
Race, ethnic Han, n (%)	264.00 (97.78%)	281.00 (96.56%)	0.388	101.00 (99.02%)	97.00 (95.10%)	0.098
Baseline APECH-II (Median, IQR)	26.50 (23.00, 28.00)	17.00 (13.00, 22.00)	0.000*	24.00 (19.00, 26.50)	22.00 (19.00, 27.00)	0.901
Baseline CCI Median IQR	5 (4, 6)	6 (5, 8)	0.000*	5 (4, 6)	5 (4, 7)	0.662
Baseline Lab examinations						
CRP, Median IQR	44.42 (10.05, 99.65)	50.96 (10.36, 118.20)	0.541	32.84 (6.41, 81.90)	43.23 (8.95, 100.66)	0.300
PCT, Median IQR	0.26 (0.10, 1.33)	0.20 (0.07, 0.92)	0.018	0.24 (0.09, 1.33)	0.24 (0.06, 0.92)	0.236
WBC, Median IQR	9.07 (6.73, 13.61)	9.45 (6.72, 13.17)	0.950	9.01 (6.76, 13.60)	9.94 (6.90, 13.17)	0.621
NE%, Median IQR	85.15 (77.00, 90.10)	84.40 (75.60, 90.40)	0.752	85.45 (75.30, 90.00)	82.65 (74.70, 89.30)	0.203
Main infectious diseases, n	927	1006	0.317	399	412	0.317
Bacterial pneumonia (J15.901*), n (%)	249 (26.86%)	323 (32.11%)		109 (27.32%)	123 (29.85%)	
Sepsis (A41.902*), n (%)	232 (25.03%)	245 (24.35%)		100 (25.06%)	98 (23.79%)	
Urinary infection (N39.001*), n (%)	133 (14.35%)	132 (13.12%)		58 (14.54%)	56 (13.59%)	

Septic shock (A41.903*), n (%)	107 (11.54%)	93 (9.24%)	43 (10.78%)	46 (11.17%)
Fungal pneumonia (B49xx20*), n (%)	54 (5.83%)	58 (5.77%)	21 (5.26%)	24 (5.83%)
Fungal urinary infection (B49xx04*), n (%)	28 (3.02%)	22 (2.19%)	11 (2.76%)	8 (1.94%)

* ICD 10 code

3.2 Activities of clinical pharmacists

A total of 862 pharmacist-recommendations were identified, of which consensus made between the pharmacist and the ICU physicians was 833 (96.64%). The top 5 recommendations mostly occurred by the ICU pharmacist were medication regimen adjustments by diseases on progression (180/862, 20.88%) with 95.00% acceptance rate (171/180), medication regimen adjustments by microbial results (170/862, 19.72%) with 95.88% acceptance rate (163/170), drug withdrawal by full treatment courses (114/862, 13.23%) with 96.49% acceptance rate (110/114), suggestions for TDM (103/862, 11.95%) with 98.06% acceptance rate (101/103) and medication regimen adjustments by de-escalation (75/862, 8.70%) with 100.00% acceptance rate (75/75). The details were shown in table 2.

Tab 2

Top 5 pharmacist activities mostly occurred and the acceptance by the ICU clinicians

No.	Contents	No.	Proportion (%)	Consensus No. with ICU physicians	Acceptance (%)
1	Medication regimen adjustments by diseases on progression	180	20.88%	171	95.00%
2	Medication regimen adjustments by microbial results	170	19.72%	163	95.88%
3	Drug withdrawal by full treatment courses	114	13.23%	110	96.49%
4	Suggestions for TDM*	103	11.95%	101	98.06%
5	Medication regimen adjustments by de-escalation	75	8.70%	75	100.00%

*TDM, Therapeutic drug monitoring

3.3 The positive influence to the ICU clinicians on drug selection tendency

We are interested in the impact of pharmacist intervention on antibiotic usage in ICU patients. In a summary, the AUD of all antibiotics consumed in the ICU decreased from 241.91 DDD/100 bed days to 176.64 DDD/100 bed days after implementing the intervention ($p=0.018$). By agent, AUD proportion was observed decreasingly in carbapenems (23.07% vs 14.43%), triazole and other antimycotics for systemic use (16.98% vs 18.53%), glycopeptides and linezolid (15.32% vs 14.83%), tetracyclines (11.56% vs 6.26%) and third-generation cephalosporins (6.91% vs 4.57%). The descender was 48.59%, 10.27%, 20.44%, 55.52% or 45.61%, respectively. Whereas, AUD proportion was increased in aminoglycosides (9.41% vs 11.77%), monobactams (4.76% vs 9.47%), combinations of penicillin and beta-lactamase inhibitors (3.71% vs 10.65%) and fluoroquinolones (2.42% vs 0.91%). The descender was -2.77%, -63.68%, -135.65% or -14.92%, respectively. The corresponding results were shown in Figure 2.

3.4 Clinical and economic outcomes with and without ICU pharmacists

As shown in Table 3, the ICU mortality ($p=0.607$) and LOS ($p=0.163$) with or without pharmacist exposed had no statistical difference. About the cost, pharmacist intervention significantly decreased the antibiotic charges from \$836.3 (IQR 426.88, 1682.09) to \$362.15 (IQR 148.23, 1034.4) ($p<0.001$). Correspondingly, total cost of all medications were reduced from \$2868.18 (IQR \$1268.44, \$5059.00) vs \$1941.5 (IQR \$1092.89, \$3538.97) ($p=0.016$).

Tab 3

Clinical and economic outcomes of critically ill patients with infectious diseases with and without clinical pharmacists in ICUs.

Clinical and economic outcomes	The control group	The pharmacist-exposed group	P
Mortality, No (%)	20.00 (19.61%)	23.00 (22.55%)	0.607
LOS, Median[IQR]	8.00 (5.00, 13.00)	6.90 (4.50, 12.15)	0.163
Antibiotic charges per stay (\$/case), Median[IQR]	836.3 (426.88, 1682.09)	362.15 (148.23, 1034.4)	< 0.001
Drug charges per stay (\$/case), Median [IQR]	2868.18 (1268.44, 5059.00)	1941.5 (1092.89, 3538.97)	0.016

3.5 The relationship between mortality and pharmacist interventions

Univariate analyses showed that there was no statistically difference in pharmacist intervention between the groups of survival and death ($p=0.288$), but in the factors of age ($p=0.001$), baseline APECH-II score ($p=0.029$), baseline CCI score ($p=0.032$), numbers of admissions ($p=0.001$), numbers of antibacterial drugs adoptions ($p=0.007$), numbers of antibacterial drugs combinations ($p=0.005$), discharge diagnostic items ($p<0.001$), total

number of bacteria detected ($p=0.001$), numbers of gram-positive cocci detected ($p=0.038$) and number of fungi detected ($p=0.002$) were as significant variables affecting the morality. Results of bivariate logistic regression was shown that the mortality outcome was related to the patients' numbers of admissions ($OR=1.095$, 95%CI 1.028-1.165), discharge diagnostic items ($OR=1.109$, 95%CI 1.054-1.166) and numbers of gram-positive cocci detected ($OR= 3.392$, 95%CI 1.348-8.531). The details were shown in supplement 1 and 2.

4. Discussions

Antibiotic exposure in intensive care patients is often inadequate and is associated with poor patient outcomes as critically ill patients have altered antibiotic pharmacokinetics. Clinically relevant pharmacokinetic knowledge on antibiotic dosing among intensive care professionals is insufficient [20]. This report describes the successful integration of a clinical pharmacist into ICU clinic and outlines the primary roles the pharmacist can serve within the ICU health care team, particularly in terms of cost avoidance outcomes.

There are three modes of collaboration between pharmacists and clinicians now, pharmacist-clinician cooperation, pharmacist-driven, and clinician attendance or pharmacist alone. In the ICU, because of the complexity of the patients, the severity of the disease, and the diversity of drug use, a multidisciplinary approach would be optimal [21]. During the pharmacist exposed period in this paper, the pharmacist works in the ward, reviews all the critical infectious patient medication regimens, and exchanges views with the physician about any treatment issues found. Medication regimen adjustments, the timing of antimicrobial therapy withdrawal, or TDM suggestions were the main points that the pharmacist interventions. The final treatment decision was based on full discussion and communication between the pharmacist and the physician, the consensus rate was more than 90% or higher.

Pharmacist intervention can also reduce broad-spectrum antimicrobials usage in the ICU ward. Carbapenems were used to have the highest proportion without the pharmacist attendance to ICU, whereas this proportion was lower to the third rating during the pharmacist exposure period. Tetracyclines had the sharpest decline after the pharmacist attendance, especially in tigecycline. Both descenders of carbapenems and tetracyclines were around 50%. On the contrary, the combinations therapy of penicillins and beta-lactamase inhibitors and monobactams were increasing obviously, which meant the narrower spectrum antimicrobials were trended to choose since the pharmacist recommendation.

The roles of pharmacists on the geriatric patient care had been proved by many studies [10, 22–25]. Lee et al reported that including critical care pharmacists in the multidisciplinary ICU team improved patient outcomes including mortality, ICU length of stay in mixed ICUs, and preventable/non-preventable adverse drug events [26]. In our study, after pharmacist attendance, the rate of antimicrobial agent utilization in the discharged patients decreased and patient antibiotic charges including the total drug costs were saving per stay. Meanwhile, the ICU mortality did not increase. Results of univariate analysis was also shown no statistically difference in pharmacist intervention between the groups of survival and death. LOS failed to shorten after pharmacist intervention since this indicator was always one of the important independent performance management indicators in clinic. So it might be strictly controlled independently. About the economic indicators, the costs used in this study was the absolute amounts by the patient before the medicare reimbursement. Antibiotic charges per stay of the infectious patient in the ICU ward could be decreased from

\$836.3 to \$362.15 (median charges) with 56.70% descender and the total drug charges per stay could be decreased from \$2868.18 to \$1941.50 with the 32.31% descender.

This study has several limitations. First, this intervention study was designed without involving a simultaneous control ICU group since the ICU ward in this study was the only one of comprehensive ICU in this hospital and it was difficult to find the parallel control group from another ward at the same study time to be compared. So the results in this study may be probably influenced by the period. Second, this was a single-center study. Every medical setting has different cooperation patterns between clinical pharmacists and ICU physicians, as well as different work priorities, and then leading to different roles. Therefore, our results might not be generalized to other ICU settings. Third, about the observed period, the clinical pharmacist joined ICU in 2018. In that year, the pharmacist mainly adapted to the working environment of the ward and focused on exploring the clinical pharmaceutical work, which was concerned as a transitional stage. So we didn't enrolled the annual data of 2018 as the observed period. Hence, more rigorous studies are needed to confirm the role of ICU clinical pharmacists.

5. Conclusions

In summary, this study demonstrated that the services provided by the clinical pharmacist with highly professional training in caring for critically ill patients with infections could optimize the antibiotic therapy regimes, reduced the broad-spectrum antibiotics adoptions and significantly saved the drug costs. Our conclusion also indicated that at least the reduction of antibacterial feeding intervened by the pharmacist did not cause the critical infectious patients' under-treatment and then increase the mortalities. These results need to be validated with further studies and the specific activities associated with the greatest benefit determined.

Declarations

Ethics approval and consent to participate

This study was approved by the Scientific Ethics Committee, Beijing Shijitan Hospital Affiliated to Capital Medical University [Ethics approval No: sjtky11-1x-2020(46)], and was performed in compliance with the principles of the Declaration of Helsinki. Since this was a retrospective study, written informed consent for participation was not required for this study in accordance with the national legislation and the institutional requirements.

Consent for publication

Not applicable.

Authors' contributions

WC contributed to the conception, design of the work and revised the draft. HG analyzed and interpreted the patient data. She was also a major contributor in writing the manuscript. LLS co-contributed to the design of

this study and guided data collection. BS, XYG and SZW performed the acquisition, analysis and interpretation of data. LL, as the analysts in this study, was responsible for data review and statistics check. All authors read and approved the final manuscript.

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Conflict of interest

The authors declare that they have no competing interests.

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

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References

1. Kollef MH. Optimizing antibiotic therapy in the intensive care unit setting. *Crit Care*. 2001; 5(4):189–95.
2. Kram BL, Trammel MA, Kram SJ, Wheeley SE, Mancheril BG, Burgess LD, Schultheis JM. Medication Histories in Critically Ill Patients Completed by Pharmacy Personnel. *Ann Pharmacother*. 2019; 53(6):596–602.
3. Carson-Stevens A, Hingston CD, Wise MP. Minimising drug errors in critically ill patients. *Crit Care*. 2011; 15(1):401.
4. Kollef MH. Antibiotics for the critically ill: more than just selecting appropriate initial therapy. *Crit Care*. 2013; 17(3):146.
5. Warden BA, Shapiro MD, Fazio S. The Role of the Clinical Pharmacist in a Preventive Cardiology Practice. *Ann Pharmacother*. 2019; 53(12):1214–9.
6. American Pharmacists A. DOTx. MED: Pharmacist-delivered interventions to improve care for patients with diabetes. *J Am Pharm Assoc (2003)*. 2012; 52(1):25-33.

7. Falamic S, Lucijanac M, Hadziabdic MO, Marusic S, Bacic Vrca V. Pharmacist's interventions improve time in therapeutic range of elderly rural patients on warfarin therapy: a randomized trial. *Int J Clin Pharm*. 2018; 40(5):1078–85.
8. Montazeri M, Cook DJ. Impact of a clinical pharmacist in a multidisciplinary intensive care unit. *Crit Care Med*. 1994; 22(6):1044–8.
9. Alvarez-Lerma F, Grau S, Echeverria-Esnal D, Martinez-Alonso M, Gracia-Arnillas MP, Horcajada JP, Masclans JR. A Before-and-After Study of the Effectiveness of an Antimicrobial Stewardship Program in Critical Care. *Antimicrob Agents Chemother*. 2018; 62(4):e01825-17.
10. DiazGranados CA. Prospective audit for antimicrobial stewardship in intensive care: impact on resistance and clinical outcomes. *Am J Infect Control*. 2012; 40(6):526–9.
11. Stollings JL, Bloom SL, Wang L, Ely EW, Jackson JC, Sevin CM. Critical Care Pharmacists and Medication Management in an ICU Recovery Center. *Ann Pharmacother*. 2018; 52(8):713–23.
12. MacLaren R, Bond CA, Martin SJ, Fike D. Clinical and economic outcomes of involving pharmacists in the direct care of critically ill patients with infections. *Crit Care Med*. 2008; 36(12):3184–9.
13. Miyagawa CI, Rivera JO. Effect of pharmacist interventions on drug therapy costs in a surgical intensive-care unit. *Am J Hosp Pharm*. 1986; 43(12):3008–13.
14. Leape LL, Cullen DJ, Clapp MD, Burdick E, Demonaco HJ, Erickson JI, Bates DW. Pharmacist participation on physician rounds and adverse drug events in the intensive care unit. *JAMA*. 1999; 282(3):267–70.
15. Cai Li-jian ZQ-z, Peng Wen-xing, He Da-ren. Retrospect and prospect of the development of clinical pharmacy in China. *Medicine and philosophy*. 2010; 31 (9):79–80.
16. Guidelines for ATC classification and DDD assignment. 2021. URL: https://www.whocc.no/filearchive/publications/2021_guidelines_web.pdf. Accessed 25 July 2021.
17. ATC/DDD Index. 2021. URL: https://www.whocc.no/atc_ddd_index. Accessed 25 Junly 2021.
18. Introduction to DDD Indicators. 2021. URL: <https://www.who.int/tools/atc-ddd-toolkit/indicators>. Accessed 25 July 2021.
19. Surveillance of Antimicrobial Use. 2021. URL: https://www.who.int/medicines/areas/rational_use/AMU_Surveillance/en/. Accessed 25 Junly 2021.
20. Fleuren LM, Roggeveen LF, Guo T, Waldauf P, van der Voort PHJ, Bosman RJ, Swart EL, Girbes ARJ, Elbers PWG. Clinically relevant pharmacokinetic knowledge on antibiotic dosing among intensive care professionals is insufficient: a cross-sectional study. *Crit Care*. 2019; 23(1):185.
21. Ibrahim KH, Gunderson B, Rotschafer JC. Intensive care unit antimicrobial resistance and the role of the pharmacist. *Crit Care Med*. 2001; 29(4 Suppl):N108-13.
22. Diane M Parente JM. Role of the Pharmacist in Antimicrobial Stewardship. *Med Clin North Am*. 2018; 102(5):929–36.
23. Kwak SH, Jeong CW, Lee SH, Lee HJ, Koh Y. Current status of intensive care units registered as critical care subspecialty training hospitals in Korea. *Journal of Korean medical science*. 2014; 29(3):431–7.
24. MacLaren R, Bond CA. Effects of pharmacist participation in intensive care units on clinical and economic outcomes of critically ill patients with thromboembolic or infarction-related events. *Pharmacotherapy*. 2009; 29(7):761–8.

25. Leguelinel-Blache G, Nguyen TL, Louart B, Poujol H, Lavigne JP, Roberts JA, Muller L, Kinowski JM, Roger C, Lefrant JY. Impact of Quality Bundle Enforcement by a Critical Care Pharmacist on Patient Outcome and Costs. Crit Care Med. 2018; 46(2):199–207.

26. Lee H, Ryu K, Sohn Y, Kim J, Suh GY, Kim E. Impact on Patient Outcomes of Pharmacist Participation in Multidisciplinary Critical Care Teams: A Systematic Review and Meta-Analysis. Crit Care Med. 2019; 47(9):1243–50.

Figures

Figure 1

Number of patients included and reasons for exclusions.

Main catalogies (ATC classifications*)	AUD in the control group	AUD in the pharmacist-exposed group	P value	AUD Proportion	Descender (%)
Total	214.91	176.64	0.018 [§]		
Carbapenems (J01DH)	49.57	25.49		23.07% 14.43%	48.58%
Triazole derivatives (J02AC) and Other antimycotics for systemic use (J02AX)	36.48	32.73		16.98% 18.53%	10.27%
Glycopeptides (J01XA) and linezolid (J01XX08)	32.92	26.19		15.32% 14.83%	20.44%
Tetracyclines (J01AA)	24.84	11.05		11.56% 6.26%	55.52%
aminoglycosides (J01GB)	20.23	20.79		9.41% 11.77%	-2.77%
Third-generation cephalosporins (J01DD)	14.84	8.07		6.91% 4.57%	45.61%
Monobactams (J01DF)	10.22	16.73		4.76% 9.47%	-63.68%
combinations of penicillins and beta-lactamase inhibitors (J01CR)	7.98	18.81		3.71% 10.65%	-135.65%
Fluoroquinolones (J01MA)	6.97	8.01		3.24% 4.53%	-14.92%
Miscellaneous	5.20	1.61		2.42% 0.91%	69.04%

■ Control ■ Pharmacist exposure

Figure 2

AUD influence of the ICU clinicians on drug selection tendency

Supplementary Files

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- [Supplement1.docx](#)
- [Supplement2.docx](#)