North Clin Istanb 2024;11(5):398–405
doi: 10.14744/nci.2023.82473

Original Article INFECTIOUS DISEASES

The evaluation of potential drug–drug interactions with antibiotics in hospitalized patients

Nurten Nur Aydin, Murat Aydin

Department of Infectious Diseases and Clinical Microbiology, Erzurum Regional Training and Research Hospital, Erzurum, Turkiye

ABSTRACT

OBJECTIVE: Drug-drug interactions (DDIs) occur when one drug alters the effect of another drug. The aim of this study was to evaluate potential drug-drug interactions (pDDIs) associated with the use of systemic antibiotics in hospitalized patients.

METHODS: The study included patients over the age of 18 who were hospitalized in our hospital on 12.07.2022 and were using at least two systemic drugs concurrently, with at least one being a systemic antibiotic. The study was conducted using the point prevalence method. The patients' medication was evaluated for pDDIs using the UpToDate®/Lexicomp® database system. According to this screening tool, pDDIs were classified into 4 groups according to their severity: B, C, D, and X, ranging from mild to severe.

RESULTS: Out of the 296 patients included in the study, at least one pDDI was detected in 190 patients (64.2%). One hundred seventy-seven patients (59.8%) had at least one pDDI with non-antibiotic drugs. Fifty-seven patients (19.3%) had at least one pDDI with antibiotics. One hundred and six patients (35.8%) had no drug interactions. Patients with pDDIs related to antibiotics had significantly higher age, number of comorbidities, total number of medications and number of antibiotics ($p=0.010$, $p=0.004$, $p<0.001$, $p<0.001$, respectively) compared to patients without pDDIs related to antibiotics (n=239). For antibiotics, potential pDDIs were observed 25, 75, 6, and 6 times in groups B, C, D, and X, respectively. Out of the total of 398 antibiotics, penicillins (24.9%, n=99) and cephalosporins (24.4%, n=97) were the most frequently used. Respectively, eight and two pDDIs were detected with these drugs. While quinolones were used 47 times (11.8%), 74 pDDIs (59.7%) were identified with quinolones. Out of the 47 patients who used quinolones, 37 had pDDIs with antibiotics. The most frequent pDDI with antibiotics was associated with the use of quinolone systemic corticosteroids (15 patients). The second most prevalent interaction involves quinolone-angiotensin converting enzyme inhibitors or angiotensin 2 receptor blockers (13 patients).

CONCLUSION: Antibiotics should be checked for pDDIs before being prescribed. While beta-lactam antibiotics are generally considered safer in terms of pDDIs, greater caution should be exercised, particularly when prescribing quinolones.

Keywords: Anti-bacterial agents; drug interactions; prescriptions.

Cite this article as: *Aydin NN, Aydin M. The evaluation of potential drug–drug interactions with antibiotics in hospitalized patients. North Clin Istanb 2024;11(5):398–405.*

Drug-drug interactions (DDIs) occur when one drug alters the activity of another drug. One systematic review and meta-analysis reported that DDIs were found in 33% of patients hospitalized in general wards and 67% of patients hospitalized in intensive care units [1]. Another study evaluating DDIs reported that, on average, a drug regimen included 6.58 drugs and 2.68 DDIs [2]. Age, presence of chronic diseases, number of drugs used, and duration of hospitalisation are factors that contribute to the frequency of drug interactions [3]. Potential drug-drug interactions (pDDIs) may cause adverse drug events (ADEs). Approximately 17% of ADEs in hospitalized patients are caused by potential drug-drug interactions (pDDIs) [4]. Furthermore, pDDIs can result in treatment failures among patients [5].

Received: August 23, 2023 *Revised:* September 26, 2023 *Accepted:* October 18, 2023 *Online:* October 01, 2024

Correspondence: Nurten Nur AYDIN, MD. Erzurum Bolge Egitim ve Arastirma Hastanesi, Enfeksiyon Hastaliklari ve Klinik Mikrobiyoloji Klinigi, Erzurum, Turkiye.
Tel: +90 442 432 00 00 e-mail: nurtennurkenc@hotmail.com

Istanbul Provincial Directorate of Health - Available online at www.northclinist.com

Antibiotics can also lead to pDDIs [6,7]. A recent study showed that antibiotic use in hospitalized patients ranged from 14% to 73% [8]. Hospitalized patients with infections frequently require polypharmacy because of their underlying comorbidities. Additionally, they receive supportive medications that relieve clinical complaints caused by infection. Clinicians should take pDDIs into consideration when planning the treatment of these patients. A multicenter study conducted in Turkiye found that more than 25% of pDDIs were attributed to antibiotics [9].

Numerous studies on pDDIs can be found in the literature. However, there is limited data on direct studies regarding antibiotic interactions. The aim of our study was to evaluate the pDDIs associated with the use of systemic antibiotics in hospitalized patients.

Highlight key points

- 64.2% of the patients had a pDDI with any drug and 19.3% had a pDDI with an antibiotic.
- Quinolones were prescribed to only 15.8% of patients. However, they were responsible for 59.7% of antibiotic-related pDDIs.
- The most frequent potential pDDI with antibiotics was associated with the use of quinolone - systemic corticosteroids.

MATERIALS AND METHODS

This study was conducted on 12/07/2022 using the point prevalence method in patients hospitalized at Erzurum Regional Training and Research Hospital. The study included patients over 18 years of age who simultaneously used at least two systemic drugs, with at least one being a systemic antibiotic. The data were collected from the patients' medical records and bedside observation forms. Data on age, sex, underlying disease, hospitalization unit (medical service, surgical service, intensive care unit), and all drug treatments were recorded. The UpToDate®/Lexicomp® database system (Wolters Kluwer Clinical Drug Information, Inc., last accessed 25 June 2023) was used to screen all drugs for pDDIs. This screening tool categorizes pDDIs into 5 levels of severity and also provides advice on how to manage them. These are A (no interaction), B (mild interaction, no action required), C (moderate interaction, monitor treatment to avoid potential adverse events), D (severe interaction, consider treatment modification) and X (contraindicated, avoid combination). According to this screening tool, pDDIs were classified into 4 groups as B, C, D and X. The study was approved by the Erzurum Regional Training and Research Hospital Clinical Research Ethics Committee (decision no: 2022/08-106, date: 20.06.2022) and was conducted in accordance with the principles of the Declaration of Helsinki.

Statistical Analysis

The IBM SPSS 23.0 statistical package (IBM SPSS Statistics for Windows Version 23.0, Armonk, NY: IBM Corp., USA) was used for data analysis. Descriptive statistics included number (n) and percentage (%) values for categorical variables and mean plus standard deviation (SD) values for numerical variables. The Chi-square test was used to analyze categorical variables in independent groups. The Shapiro-Wilk W test and the Kolmogorov-Smirnov test were used to assess the normal distribution of continuous variables. When comparing two independent groups, the Student t test was used for variables following a normal distribution and the Mann-Whitney U test was used for variables not following a normal distribution. The alpha level of statistical significance was accepted as $p<0.05$.

RESULTS

The study included 296 patients. Of the patients, 51.0% (n=151) were male and 49.0% (n=145) were female. The mean age of the patients was 59.6±20.0 years. Table 1 shows data on age, gender, comorbidity, hospitalized ward or intensive care unit, the number of drugs used, and the number of antibiotics used. Table 1 presents the comparison between patients with and without antibiotic-related PDDIs. The mean age was higher in patients with antibiotic-related PDDIs ($p<0.010$). A significant difference was found between the two groups in terms of the clinical units, (wards, intensive care units) in which the patients were hospitalized ($p<0.001$). Patients with antibiotic-related pDDIs were mostly hospitalized in internal wards (47.4%), while patients without antibiotic-related pDDIs were mostly hospitalized in surgical wards (51.0%). The number of comorbidities, total medications, and antibiotics used were significantly higher ($p=0.004$, $p<0.001$, $p<0.001$, respectively) in the group with antibiotic-related pDDIs.

One hundred and ninety patients (64.2%) exhibited at least one pDDI. Fifty-seven patients (19.3%) had at least one pDDI with antibiotics. One hundred and seventy-seven patients (59.8%) had at least one pDDI with non-antibiotic drugs. No pDDI occurred in 106 patients (35.8%). The patients received a total of 1931 drugs, of which 398 (20.6%) were antibiotics. The median number

Table 1. Comparison of patients with and without potential drug-drug interactions with antibiotics

	Total (n=296) (%)	Patients with antibiotic-related pDDIs (n=57) (%)	Patients without antibiotic-related pDDIs (n=239) (%)	p
Male	51.0	59.6	49.0	0.192
Female	49.0	40.4	51.0	
Mean, age±SD	59.6±20.0	65.6±19.2	58.2±20.0	**0.010**
Hospital unit where patients are hospitalized				<**0.001**
The surgical ward	44.9	19.3	51.0	
The internal ward	29.1	47.4	24.7	
The intensive care unit	26.0	33.3	24.3	
Comorbidity				
Hypertension	30.4	35.1	29.3	0.487
Cardiovascular disease	20.9	28.1	19.2	0.197
COPD	19.3	31.6	16.3	**0.015**
Diabetes mellitus	14.5	28.1	11.3	**0.003**
Malignancy	11.5	3.5	13.4	0.061
Chronic renal failure	3.7	8.8	2.5	**0.040**
Other diseases	14.9	15.8	14.6	0.991
Number of comorbidities, Mean±SD	1.2±1.2	1.5±1.1	1.1±1.2	**0.004**
Total number of drugs used by patients, Mean±SD	6.5±3.2	8.0±3.0	6.2±3.2	<**0.001**
Number of antibiotics used by a patient				<**0.001**
1	68.6	36.8	76.2	
2	29.1	54.4	23.0	
3	2.4	8.8	0.8	

SD: Standard deviation.

Table 2. Number of potential drug-drug interactions of antibiotics and other drugs in groups B, C, D and X

	B	C	D	X	Total interaction (%)
Interaction of antibiotics	25	75	6	6	11.5
Other drug interactions	163	511	168	20	88.5
Total	188	586	174	26	974 (100.0)

of administered drugs and antibiotics per patient was 6 (minimum: 2, maximum: 16) and 1 (minimum: 1, maximum: 3), respectively. A total number of 974 pDDIs were observed, out of which 112 (11.5%) were antibiotic-related pDDIs and 862 (88.5%) were non-antibiotic drug interactions (Table 2). Among antibiotic-related pDDIs, interactions of groups C and B were observed most frequently (75 and 25 times, respectively).

Penicillins (24.9%, n=99) and cephalosporins (24.4%, n=97) were the most commonly used antibiotics. There were eight and two pDDIs with these drugs, respectively. Quinolones were administered 47 times (11.8%), but 74 pDDIs were identified with quinolones (Table 3). Quinolones represented 59.7% (n=74) of all pDDIs related to antibiotics. Among quinolones, moxifloxacin was used in 23 patients, ciprofloxacin in 13 patients and levofloxacin in 11 patients.

TABLE 3. Number of potential drug-drug interactions of the antibiotics

Antibiotic group	Number of uses (%)	B n	C n	D n	X n
Penicillin	24.9	–	8	–	–
Cephalosporin	24.4	–	1	–	1
Carbapenem	13.1	–	–	–	–
Quinolone	11.8	21	46	6	1
Metronidazole	7.8	3	1	–	1
Glycopeptide	5.3	–	1	–	–
Tigecycline	5.3	–	5	–	–
Linezolid	1.8	–	5	–	2
Fosfomycin	1.5	–	–	–	–
Aminoglycoside	1.5	1	6	–	–
Clindamycin	1.0	1	–	–	–
Colistin/polymyxin B	0.5	–	–	–	–
Doxycycline	0.5	–	4	–	–
Rifampicin	0.5	1	7	–	1
Clarithromycin	0.3	–	1	–	–
Total	398 (100.0%)	27*	85*	6	6

*: The actual numbers of potential drug-drug interactions in groups B and C are lower (25 for group B and 75 for group C), but these numbers are higher in the table because antibiotics also interact among themselves.

Table 4 shows the three most frequently observed pDDIs with antibiotics. Quinolone-systemic corticosteroid interaction was the most frequent pDDI with antibiotics observed, affecting 15 patients. In 13 patients, the second most frequent interaction observed was between quinolone and renin angiotensin system blockers. Among the renin angiotensin system blockers, seven were angiotensin-converting enzyme inhibitors (ACEI), and six were angiotensin 2 receptor blockers (ARB).

Figure 1 shows the number of patients using antibiotics who encountered pDDIs with antibiotics. Out of the 47 patients who used quinolones, 37 showed pDDIs with antibiotics.

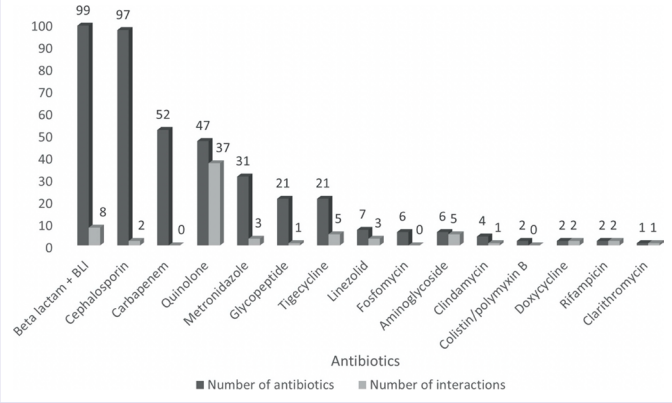

FIGURE 1. The number of antibiotics and the number of potential drug-drug interactions with these antibiotics.

BLI: Beta-lactamase inhibitor.

DISCUSSION

In this study, 64.2% of patients had pDDIs with any drug and 19.3% had pDDIs with antibiotics. The most commonly used antibiotics were penicillins and cephalosporins (in total 66.2%). Although quinolones were prescribed to only 15.8% of the patients, they were responsible for 59.7% of pDDIs related to antibiotics.

Hospitalized patients receiving antibiotics are exposed to many drugs at the same time because of the drugs they are taking for their underlying medical conditions and the symptomatic and supportive drug therapies they are receiving. It is known that the number of drugs used concomitantly in patients is a risk factor for pDDI [10]. It has also been shown that the risk of pDDI increases with the age of the patient and the number of co-morbidities [11]. A study of older people with Alzheimer's disease found that the

Table 4. Top three most common potential drug-drug interactions with antibiotics in each group

Antibiotic - Drug interaction	Kind of interaction	Possible result of interaction	Number
Group B interaction			
Quinolone - ACEI*	Increasing the risk of side effect	ACEI may increase the arrhythmogenic effect of quinolones. Quinolones may increase the nephrotoxic effect of ACEI.	7
Quinolone - ARB**	Increasing the risk of side effect	ARB may increase the arrhythmogenic effect of quinolones. Quinolones may increase the nephrotoxic effect of ARB.	6
Quinolone - metoclopramide***	Increasing the risk of side effect	They can enhance each other's QT prolonging effect.	5
Group C interaction			
Quinolone - systemic corticosteroid+	Increasing the risk of side effect	Corticosteroids may increase the toxic effects of quinolones. Specifically, they may increase the risk of tendonitis and tendon rupture	15
Quinolone - antidiabetic drug++	Enhancing and reducing drug effect	Quinolones may increase the hypoglycemic effect of antidiabetic drugs. Quinolones may reduce the therapeutic effect of antidiabetic drugs.	7
Quinolone - NSAIDs+++	Increasing the risk of side effect	NSAIDs increase the neuroexcitatory and/or seizure-inducing effect of quinolones.	7
Group D interaction			
Moxifloxacin - magnesium oxide	Reducing drug concentration	Magnesium salts can reduce the serum concentration of quinolones	3
Levofloxacin - magnesium oxide	Reducing drug concentration	Magnesium salts can reduce the serum concentration of quinolones	2
Ciprofloxacin - sucralfate	Reducing drug concentration	Sucralfate may decrease the serum concentration of quinolones	1
X group interaction			
Linezolid - metoclopramide	Increasing the risk of side effect	Metoclopramide may increase the hypertensive effect of linezolid	2
Cefuroxime - pantoprazole	Reducing drug concentration	Pantoprazole may reduce the oral absorption of cefuroxime	1
Levofloxacin - amiodarone	Increasing the risk of side effects	Levofloxacin may increase the QT prolongation effect of amiodarone	1

ACEI: Angiotensin-converting enzyme inhibitors; ARB: Angiotensin 2 receptor blockers; NSAIDs: Non-steroidal anti-inflammatory drugs; *: Moxifloxacin-perindopril 2 times, moxifloxacin ramipril 2 times, moxifloxacin captopril 1 time, ciprofloxacin-ramipril 1 time, ciprofloxacin-captopril 1 time; **: Levofloxacin-valsartan 2 times, levofloxacin-olmesartan 1 time, moxifloxacin-candesartan 1 time, moxifloxacin-valsartan 1 time, ciprofloxacin-candesartan 1 time; ***: 3 times with levofloxacin, 2 times with moxifloxacin; +: Moxifloxacin-methylprednisolone 7 times, levofloxacin-methylprednisolone 5 times, moxifloxacin-dexamethasone 2 times, ciprofloxacin-methylprednisolone 1 time; ++: Insulin aspart 2 times, insulin glargine 2 times, merformin 1 time, sitagliptin 1 time, glyclazide 1 time from antidiabetic drugs; +++: Ciprofloxacin-tenoxicam 4 times, ciprofloxacin dexketoprofen 2 times, levofloxacin- tenoxicam 1 time.

risk of pDDIs increases as the number of comorbid conditions increases [12]. Our study shows that patients with pDDIs had significantly higher mean age, number of comorbidities, and total medications used. It is important to be vigilant about drug interactions in hospitalized patients, especially those who are older, have multiple comorbidities, and use multiple medications.

The occurrence rate of pDDIs in hospitalized patients ranges between 33–67% [1, 9]. We found 64.2% of patients with pDDIs in our study. All patients in our study were receiving antibiotic treatment, which may have contributed to the high prevalence of pDDIs. Antibiotics are among the leading drug groups in pDDIs studies. A multicenter study conducted in hospitalized patients revealed that pDDIs involving antibiotics constituted 26.4% of all

recorded interactions [9]. Another point prevalence study found that over 25% of drug interactions were associated with antibiotics [13]. In our study, pDDIs with antibiotics were observed in 19.3% of patients. Clinicians should be aware of the possibility of drug interactions when prescribing antibiotics, as with any other medication. Our study revealed an association between an increase in the number of antibiotics administered and an increase in the incidence of drug interactions. Kuscu et al. [9] also found that the risk of pDDI with antibiotics increased with the number of antibiotics administered. Hence, when possible, antibiotic treatments should be simplified and monotherapy should be preferred to reduce the risk of pDDI with antibiotics.

The antibiotic group most widely used in our study were penicillins and cephalosporins, but pDDIs were more frequent with quinolones. The most prevailing drug combination leading to pDDIs in patients was the use of quinolones and systemic corticosteroids. The quinolone and renin angiotensin system blockers (ACEI or ARB) combination was the second most frequent. Other pDDIs were observed with the use of quinolones with antidiabetic drugs and with non-steroidal anti-inflammatory drugs. Given that the study was conducted during the coronavirus pandemic, there was an increase in the number of hospitalized patients with pneumonia. The combination of quinolones and systemic corticosteroids was the most common drug combination in our study, as respiratory quinolones were frequently administered to these patients and systemic corticosteroids were administered for supportive treatment due to hypoxia. Quinolones are known to cause tendinitis and tendon rupture [14]. Systemic corticosteroids may exacerbate this adverse effect of quinolones [14, 15]. In a study evaluating the risk of pDDIs in COVID-19 patients treated with corticosteroids, it was reported that the risk of tendon rupture increased in 2% of patients with the combined use of corticosteroids and quinolones [16]. Fifteen patients in our study used quinolones and systemic corticosteroids concomitantly. Patients should be advised to discontinue quinolones, rest, not exercise, and consult their physician if any signs of tendinopathy (e.g. pain, swelling) develop, while using quinolones [17]. Additionally, patients who use systemic corticosteroids and quinolones together should be closely monitored for the risk of tendinopathy.

Quinolones have drug interactions with several medications. Quinolones may increase the duration of the QT interval by inhibiting cardiac potassium voltage-gated channels [18]. As a result, concurrent administration with other drugs that can prolong the QT interval must be avoided whenever feasible. Moxifloxacin has the greatest association with cardiac arrhythmia and QT prolongation among quinolones, followed by levofloxacin and ciprofloxacin [19]. In our study, moxifloxacin was the most frequently prescribed quinolone (23 patients). Thirteen patients received ciprofloxacin, while eleven patients were treated with levofloxacin. According to Table 4 of the study findings, moxifloxacin was the drug most commonly associated with drug interactions that cause cardiac arrhythmia side effects. In our study, the combination of quinolones with renin-angiotensin system blockers (ACEI or ARB) was the second most common cause of pDDIs. There is evidence that renin-angiotensin system blockers can increase the risk of cardiac arrhythmia side effects associated with quinolones. Quinolones could increase the nephrotoxic effect of renin angiotensin system blockers by 4.5 times [20]. Administration of ciprofloxacin to patients receiving renin angiotensin system blockers has been reported to be linked with an elevated risk of sudden death [21]. The mechanism of this phenomenon is not yet fully understood. It is unclear, but it is a fact that ciprofloxacin prolongs the QT interval and has arrhythmic side effects. The use of ciprofloxacin with a drug that causes hyperkalemia may increase this arrhythmic side effect [21]. Other quinolones such as levofloxacin and moxifloxacin also have QT prolonging effects, and thus the same risk may apply to them as well. If renin angiotensin system blockers and quinolones are simultaneously used, it may be appropriate to conduct closer monitoring of renal function and cardiac rhythm.

The effects of antidiabetic drugs on blood glucose may be altered when taken with quinolones. These drugs can cause both an increase in hypoglycemic effects and a decrease in therapeutic effects, as well as hyperglycemia, when taken with quinolones [22, 23]. It is recommended to closely monitor the blood glucose levels of patients taking quinolones in combination with antidiabetic drugs, due to the risk of hypo- or hyperglycemia. In general, hypoglycemia is more likely to occur within the first one or two days of taking antibiotics, whereas hyperglycemia tends to occur later in the course of treatment [22, 23]. Co-administration of quinolone antidiabetic drugs occurred seven times in our study.

Co-administration of quinolones and non-steroidal anti-inflammatory drugs (NSAIDs) may increase the risk of central nervous system (CNS) stimulation and seizures in patients [24, 25]. In our study, 7 patients were receiving concomitant quinolone and NSAID therapy. It is important to consider that concomitant use of quinolones and NSAIDs may increase the risk of seizures in patients. The risk of seizures is particularly higher in patients with

a medical history of seizures, renal impairment, or those taking other drugs that have a lower seizure threshold [26].

The concomitant use of linezolid and metoclopramide is contraindicated in Category X due to the risk of severe hypertension [27]. It is recommended to avoid concomitant use of metoclopramide and linezolid. In our study, two patients had concomitant use of metoclopramide and linezolid.

Concomitant use of levofloxacin and amiodarone should be avoided as both cause prolongation of the QT interval [28, 29]. According to the prescribing information for levofloxacin, it should not be used concomitantly with antiarrhythmic drugs such as amiodarone, as this can lead to prolongation of the QT interval and torsades de pointes [30]. One patient in our study was receiving these two drugs together.

The absorption of cefuroxime may be reduced by Proton Pump Inhibitors. A study showed that the area under the curve decreased by over 60% when cefuroxime was administered simultaneously with ranitidine and sodium bicarbonate [31]. The prescription information of cefuroxime axetil recommends that it should not be taken with proton pump inhibitors as these drugs may lower gastric acidity, hence reducing the absorption of cefuroxime [32]. One patient in our study took pantoprazole and cefuroxime axetil tablets simultaneously.

This study has limitations. The study detected potential drug interactions; however, it did not provide information about the actual interactions observed in the clinic. Conducting further studies that provide data on both potential drug interactions and actual interactions observed in clinical settings could be useful. Being a point prevalence study, the study reflects the current situation only and not a longer time period. Conducting studies over a longer period of time could be more insightful than conducting a point prevalence study. The potential drug interactions were evaluated only using the Lexicomp® database system. A more comprehensive evaluation can be conducted by using other databases.

Conclusion

Antibiotics are among the leading drugs in drug interactions and all antibiotics should be assessed for pDDIs before prescribing. While beta-lactam antibiotics are generally considered to be less prone to pDDIs, it is important to exercise more caution, particularly when prescribing quinolones. Integration of databases that automatically evaluate pDDIs into hospital information management systems or active involvement of clinical pharmacologists in the process in hospitals may be beneficial to reduce PDDIs in case clinicians overlook drug interactions.

Ethics Committee Approval: The Erzurum Regional Training and Research Hospital Clinical Research Ethics Committee granted approval for this study (date: 20.06.2022, number: 2022/08-106).

Authorship Contributions: Concept – NNA; Design – NNA, MA; Supervision – NNA; Fundings – NNA; Materials – MA; Data collection and/or processing – NNA; Analysis and/or interpretation – MA; Literature review – MA; Writing – NNA; Critical review – MA.

Conflict of Interest: No conflict of interest was declared by the authors.

Use of AI for Writing Assistance: Not used.

Financial Disclosure: The authors declared that this study has received no financial support.

Peer-review: Externally peer-reviewed.

REFERENCES

1. Zheng WY, Richardson LC, Li L, Day RO, Westbrook JI, Baysari MT. Drug-drug interactions and their harmful effects in hospitalised patients: a systematic review and meta-analysis. Eur J Clin Pharmacol 2018;74:15–27. [CrossRef]
2. Butkiewicz M, Restrepo NA, Haines JL, Crawford DC. Drug-drug interaction profiles of medication regimens extracted from a de-identified electronic medical records system. AMIA Jt Summits Transl Sci Proc 2016;2016:33–40.
3. Jain S, Jain P, Sharma K, Saraswat P. A Prospective analysis of drug interactions in patients of intensive cardiac care unit. J Clin Diagn Res 2017;11:FC01–4. [CrossRef]
4. Krähenbühl-Melcher A, Schlienger R, Lampert M, Haschke M, Drewe J, Krähenbühl S. Drug-related problems in hospitals: a review of the recent literature. Drug Saf 2007;30:379–407. [CrossRef]
5. Uijtendaal EV, van Harssel LL, Hugenholtz GW, Kuck EM, Zwart-van Rijkom JE, Cremer OL, et al. Analysis of potential drug-drug interactions in medical intensive care unit patients. Pharmacotherapy 2014;34:213–9. [CrossRef]
6. Bjerrum L, Gonzalez Lopez-Valcarcel B, Petersen G. Risk factors for potential drug interactions in general practice. Eur J Gen Pract 2008;14:23–9. [CrossRef]
7. Dai D, Feinstein JA, Morrison W, Zuppa AF, Feudtner C. Epidemiology of polypharmacy and potential drug-drug interactions among pediatric patients in ICUs of U.S. Children's hospitals. Pediatr Crit Care Med 2016;17:e218–28. [CrossRef]
8. Anugulruengkitt S, Charoenpong L, Kulthanmanusorn A, Thienthong V, Usayaporn S, Kaewkhankhaeng W, et al. Point prevalence survey of antibiotic use among hospitalized patients across 41 hospitals in Thailand. JAC Antimicrob Resist 2023;5:dlac140. [CrossRef]
9. Kuscu F, Ulu A, Inal AS, Suntur BM, Aydemir H, Gul S, et al. Potential drug-drug interactions with antimicrobials in hospitalized patients: a multicenter point-prevalence study. Med Sci Monit 2018;24:4240–7. [CrossRef]
10. Khandeparkar A, Rataboli PV. A study of harmful drug-drug interactions due to polypharmacy in hospitalized patients in Goa Medical College. Perspect Clin Res 2017;8:180–6. [CrossRef]
11. Janković SM, Pejčić AV, Milosavljević MN, Opančina VD, Pešić NV, Nedeljković TT, et al. Risk factors for potential drug-drug interactions in intensive care unit patients. J Crit Care 2018;43:1–6. [CrossRef]
12. Savran M, Aşçı H, Sengeze N, Onal Ö, Demirci S. The potential drug-drug ınteractions in Alzheimer patients' treatment. Suleyman Demirel Univ Inst Health Sci 2019;10:381–8.

13. Akdemir Kalkan İ, Çınar G, Pehlivanlı A, Ürkmez F, Topaloğlu İE, Akyol B, et al. Pattern of systemic antibiotic use and potential drug interactions: evaluations through a point prevalence study in Ankara University Hospitals. Turk J Med Sci 2021;51:523–9. [CrossRef]
14. Wise BL, Peloquin C, Choi H, Lane NE, Zhang Y. Impact of age, sex, obesity, and steroid use on quinolone-associated tendon disorders. Am J Med 2012;125:1228.e23–8. [CrossRef]
15. Seeger JD, West WA, Fife D, Noel GJ, Johnson LN, Walker AM. Achilles tendon rupture and its association with fluoroquinolone antibiotics and other potential risk factors in a managed care population. Pharmacoepidemiol Drug Saf 2006;15:784–92. [CrossRef]
16. Cattaneo D, Pasina L, Conti F, Giacomelli A, Oreni L, Pezzati L, et al. Risks of potential drug-drug interactions in COVID-19 patients treated with corticosteroids: a single-center experience. J Endocrinol Invest 2021;44:2849–51. [CrossRef]
17. US Food and Drug Administration. FDA Drug Safety Communication: FDA updates warnings for oral and injectable fluoroquinolone antibiotics due to disabling side effects. Available at: https://www.fda.gov/drugs/drug-safety-and-availability/fda-drug-safety-communication-fda-updates-warnings-oral-and-injectable-fluoroquinolone-antibiotics Accessed Sep 2, 2024.
18. Kang J, Wang L, Chen XL, Triggle DJ, Rampe D. Interactions of a series of fluoroquinolone antibacterial drugs with the human cardiac K+ channel HERG. Mol Pharmacol 2001;59:122–6. [CrossRef]
19. Gorelik E, Masarwa R, Perlman A, Rotshild V, Abbasi M, Muszkat M, et al. Fluoroquinolones and cardiovascular risk: a systematic review, meta-analysis and network meta-analysis. Drug Saf 2019;42:529–38. [CrossRef]
20. Bird ST, Etminan M, Brophy JM, Hartzema AG, Delaney JA. Risk of acute kidney injury associated with the use of fluoroquinolones. CMAJ 2013;185:E475–82. [CrossRef]
21. Fralick M, Macdonald EM, Gomes T, Antoniou T, Hollands S, Mamdani MM, et al; Canadian Drug Safety and Effectiveness Research Network. Co-trimoxazole and sudden death in patients receiving inhibitors of renin-angiotensin system: population based study. BMJ 2014;349:g6196. [CrossRef]
22. Lodise T, Graves J, Miller C, Mohr JF, Lomaestro B, Smith RP. Effects of gatifloxacin and levofloxacin on rates of hypoglycemia and hyperglycemia among elderly hospitalized patients. Pharmacotherapy 2007;27:1498–505. [CrossRef]
23. Graumlich JF, Habis S, Avelino RR, Salverson SM, Gaddamanugu M, Jamma K, et al. Hypoglycemia in inpatients after gatifloxacin or levofloxacin therapy: nested case-control study. Pharmacotherapy 2005;25:1296–302. [CrossRef]
24. Mizuno J, Sugimoto S, Kaneko A, Tsutsui T, Tsutsui T, Zushi N, et al. Convulsion following the combination of single preoperative oral administration of enoxacine and single postoperative intravenous administration of flurbiprofen axetil. [Article in Japanese]. Masui 2001;50:425–8.
25. Shrivastava MP, Makde SD, Paranjpe BD. Interaction of ciprofloxacin with diclofenac and paracetamol in relation to it's epileptogenic effect. Indian J Physiol Pharmacol 1997;41:164–6.
26. Kushner JM, Peckman HJ, Snyder CR. Seizures associated with fluoroquinolones. Ann Pharmacother 2001;35:1194–8. [CrossRef]
27. Reglan (metoclopramide). Highlights of prescribing information. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/017854s062lbl.pdf. Accessed Sep 2, 2024.
28. Poluzzi E, Raschi E, Motola D, Moretti U, De Ponti F. Antimicrobials and the risk of torsades de pointes: the contribution from data mining of the US FDA Adverse Event Reporting System. Drug Saf 2010;33:303–314. [CrossRef]
29. Romero J, Baldinger SH, Goodman-Meza D, Engstrom K, Valencia CR, Golive A, et al. Drug-induced torsades de pointes in an underserved urban population. Methadone: is there therapeutic equipoise? J Interv Card Electrophysiol 2016;45:37–45. [CrossRef]
30. Levaquin (levofloxacin). Highlights of prescribing information. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/020634s069lbl.pdf. Accessed Sep 2, 2024.
31. Sommers DK, van Wyk M, Moncrieff J, Schoeman HS. Influence of food and reduced gastric acidity on the bioavailability of bacampicillin and cefuroxime axetil. Br J Clin Pharmacol 1984;18:535–9. [CrossRef]
32. Ceftin (cefuroxime axetil). Prescribing information. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2007/050605s042lbl.pdf. Accessed Sep 2, 2024.