Evaluation of the Rational Use of Intravenous Clindamycin at an Academic Medical Center in Iran

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Abstract

Background: The inappropriate use of antibiotics is prevalent in low- and middle-income countries, which can lead to serious complications such as Clostridium difficile infections and antimicrobial resistance. This study aimed to evaluate the rational use of intravenous clindamycin in hospitalized patients.

Methods: A retrospective observational study was conducted to analyze the medical records of patients over 18 years old who received intravenous clindamycin. Patient characteristics, clindamycin indications, dosage, and treatment duration were recorded. Additionally, the initial diagnosis and infection type for each patient were reviewed using available information. The rational use of clindamycin was evaluated using the UpToDate® Lexidrug™ database and relevant guidelines. Data were analyzed using SPSS software.

Results: Of the 208 patients, 56% were female. The most prevalent initial diagnosis was sepsis (16.8%). More than half of the prescriptions were made by internists. Confirmed infections primarily included aspiration pneumonia (24.5%), diabetic foot infections (11.1%), and prophylaxis for gynecological surgery (10.6%). After reviewing the patients' records, it was found that 49.5% of clindamycin indications, 98.6% of dosages, and 48.6% of treatment durations were appropriate. Considering all three factors—and excluding cases involving unnecessary duplicate therapy for anaerobes or methicillin-resistant Staphylococcus aureus (MRSA), as well as those lacking adequate evidence for clindamycin use—only 25.5% of the clindamycin regimens were deemed appropriate. Mild adverse effects were reported in four patients.

Conclusion: The study revealed that only one-fourth of clindamycin use was entirely appropriate. These findings underscore the need to implement anti-anaerobic stewardship programs that consider the type of infection, standard antibiotic regimens, prophylaxis duration, and concurrent antibiotic use to promote rational antibiotic prescribing.

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Keywords: Clindamycin; Antibiotic Stewardship; Infectious Diseases

Introduction

Antibiotics are among the most commonly prescribed medications for hospitalized patients in Iran (1). However, approximately 30% of all prescribed antibiotics have been found to be unnecessary or suboptimal. The issue of inappropriate antibiotic use is particularly prevalent in low- and middle-income countries (2). Therefore, hospital antibiotic stewardship programs (ASPs) are essential for optimizing patient care. These programs play a crucial role in effectively treating infections, protecting patients from the adverse effects of unnecessary antibiotic use, and combating antibiotic resistance (3).

Clindamycin, a lincosamide antibiotic, is frequently prescribed in the Iranian inpatient population (1). It has a wide range of clinical applications, including the treatment of anaerobic, streptococcal, and staphylococcal infections. Clindamycin inhibits bacterial protein synthesis by reversibly binding to the 50S ribosomal subunit. Its effect can be either bacteriostatic or bactericidal, depending on

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the organism type and drug concentration. Additionally, clindamycin is effective against methicillin-resistant Staphylococcus aureus (MRSA) and can also be used to treat uncomplicated skin infections (4).

Several Iranian studies have documented the irrational use of clindamycin, including its prescription without confirmed bacterial infection or microbiological evidence (1,5-8). One study evaluating clindamycin stewardship found that 61% of its hospital use was inappropriate, primarily due to incorrect duration and dosage, with pneumonia being the most common off-label indication (5). It is also important to note that clindamycin contributes to Clostridioides difficile-associated diarrhea (CDAD) and severe colitis, which can be life-threatening conditions (9). Furthermore, resistance to clindamycin has become a growing global concern, with clindamycin-resistant strains responsible for over 40% of group B streptococcal infections (10). Resistance has been observed in both MRSA and methicillin-sensitive Staphylococcus aureus (MSSA) isolated from Iranian patients (11). Moreover, resistance rates are rising among anaerobic bacteria, such as the Bacteroides fragilis group and non-fragilis species (12,13). This evidence underscores the urgent need to improve clindamycin prescribing practices.

Due to the lack of a clindamycin stewardship program (and other anti-anaerobic antibiotic stewardship programs) in Iranian hospitals, this study aimed to evaluate the rational use of intravenous clindamycin. The assessment focused on its indications, dosage, and duration of treatment. Additionally, we examined adherence to evidence-based recommendations outlined in UpToDate's clindamycin drug information and related guidelines.

Methods

This retrospective, cross-sectional study was conducted at Sayad Shirazi Academic Medical Center in Gorgan, northern Iran. This hospital is a multidisciplinary care center comprising various medical departments, including internal medicine, infectious diseases, neurology, general surgery, gynecology, and the intensive care unit. Patients were selected regardless of their admitted ward. Medical records of adult patients who received intravenous clindamycin for more than 48 hours in 2022 were reviewed. The sample size was calculated using a 95% confidence level, 85% statistical power, and a 5% margin of error. The minimum sample size was 208 patients (Z = 1.96), calculated using the formula $n = (\frac{z^2 \times \rho(1-\rho)}{\varepsilon^2})$.

Data were extracted from electronic medical records and included demographic characteristics, types of infections, laboratory test results, concomitant antibiotics, clindamycin dosages, administration routes, treatment duration, incidence of hospital-acquired infections, culture results, antibiograms, length of hospital stay, and mortality rates. Prescribing practices for intravenous clindamycin—based on FDA-approved and off-label indications, as well as adherence to evidence-based recommendations—were evaluated using ©2011-2025 UpToDate® Lexidrug™, Inc. version 3.70.0 (183), as shown in Table 1.

Table 1. Intravenous clindamycin prescribing guideline

Infection	Route	Dose	Frequency	Duration	Reference
Lower respiratory tract infections	IV	600 mg	Every 8 hours	7 days	(14)
Aspiration pneumonia					
Empyema					
Lung abscess					
Skin and soft tissue infections	IV	600-900 mg	Every 8 hours	5-14 days	(15)
Diabetic foot infection					
Abscess					
Cellulitis					
Necrotizing soft tissue infection					
Gynecological infections	IV	900 mg	Every 8 hours	14 Days	(16)
Severe pelvic inflammatory diseases				Until clinical improvement	
Postpartum endometritis					
Septicemia	IV	900 mg	Every 8 hours	14 days	(17)
Bone and joint infections	IV	600-900 mg	Every 8 hours	3-4 weeks	(18)
Osteomyelitis				Osteomyelitis: 6 weeks	(19)
Septic arthritis					(20)
Toxic shock syndrome, toxin production suppression	IV	900 mg	Every 8 hours	Until clinical/ hemodynamic stability for 48-72 hours	(21)
Surgical prophylaxis	IV	900 mg	60 min prior to initial surgical incision	≤24 hours	(22)
Cesarean delivery during labor or after membrane rupture			Repeat at 6-hours interval		

IV: Intravenous.

The primary outcome was defined as the appropriate use of intravenous clindamycin according to the following criteria: correct indication for empirical therapy; appropriate definitive therapy based on microbiological results; proper choice for infection prophylaxis; appropriate dosage for each specific infection; correct duration of treatment; and avoidance of unnecessary combinations with anti-anaerobic agents (metronidazole, ampicillin-sulbactam, piperacillin-tazobactam, meropenem, imipenem) and anti-MRSA antibiotics (vancomycin, teicoplanin, linezolid), except in cases of necrotizing fasciitis and toxic shock syndrome. Any deviation from these criteria was considered inappropriate use of clindamycin. The indications for intravenous clindamycin were assessed based on documented initial diagnoses, evidence of suspected infections, empirical or definitive treatment, clinical signs and symptoms, imaging findings, and laboratory results. These assessments were then compared with established therapeutic guidelines (Table 1).
Clindamycin adverse effects were recorded only if they were confirmed and documented by healthcare providers during the hospital stay. These effects included gastrointestinal disturbances, injection site reactions, allergic responses (e.g., anaphylaxis), Clostridium difficile-associated diarrhea, and dermatologic reactions.

Ethical Considerations

Data were collected anonymously, and informed consent was obtained to use the patients' records for research purposes at the time of admission. Approval was granted by the Ethics Committee of Golestan University of Medical Sciences (Ethics code: IR.GOUMS.REC.1403.138).

Statistical Analysis

Data analysis was performed using SPSS software (version 24; SPSS Inc., Chicago, IL). Quantitative variables were presented as mean ± standard deviation (SD), while categorical variables were expressed as numbers (percentages). Categorical data were analyzed using the Chi-square test and Fisher's exact test. Pearson's chi-square test was employed to examine the association between attending physicians and adherence to appropriate clindamycin use. An independent samples t-test was used to compare data between appropriate and inappropriate clindamycin use. A two-sided p-value of less than 0.05 was considered statistically significant.

Results

A total of 208 patients were selected based on the eligibility criteria. The mean age of the patients was 59.13 ± 19.66 years (range: 18–93), and 55.8% (116) were female. The basic characteristics and clinical status of the patients are presented in Table 2. Pneumonia and sepsis were among the most frequently documented primary diagnoses. More than half of the patients (52.4%) were admitted under the care of internists, followed by obstetricians and gynecologists (18.3%) and infectious disease specialists (14.9%).

Table 2. Basic characteristics and clinical status of patients (n = 208)

Variable	n	%
Initial recorded diagnosis		
Pneumonia	46	22.1
Sepsis	35	16.8
Cesarean section	24	11.5
Diabetic foot	21	10.1
Ischemic stroke	16	7.7
Cancer complications	8	3.8
Surgical site infection	7	3.4
Other	51	24.5
Underlying Conditions		
Diabetes	134	64.4
Hypertension	130	62.5
Cardiovascular disease	62	29.8
Chronic pulmonary disease	23	11
Chronic kidney disease	17	8.2
Malignancy	16	7.7
Chronic liver disease	2	0.9
Vital Signs & Clinical Indicators		
Systolic BP < 90 mmHg	20	9.6
Need for norepinephrine	33	15.9
Tachypnea (RR > 12/min)	52	25
Tachycardia (HR > 90 bpm)	54	26
Mental Status Alteration	**74**	**35.6**
Confused	18	24.3
Drowsy	6	8.1
Lethargic	15	20.3
Agitated	16	21.6
Coma	9	12.2
Other	10	13.5
Acute kidney injury at admission	56	26.9
Prior hospitalization	43	20.7
Prior antibiotic use (during past 3 months)	48	23.1
Unspecified	29	60.4
Clindamycin	12	25.0
Cephalexin	3	6.3
Ciprofloxacin	2	4.2
Levofloxacin	2	4.2
Laboratory Test at admission	**Mean ± SD**	**Range**
ESR (mm/hr)	65 ± 34.8	0–137
CRP (mg/L)	53.8 ± 28.7	0–250
White blood cells (×10³/µL)	13.3 ± 7.4	2–68
Neutrophil percentage (%)	75.6 ± 10.1	50–96
Platelet count (×10³/µL)	237.9 ± 109.3	28–650

BP: Blood Pressure, ESR: Erythrocyte Sedimentation Rate, HR: Heart Rate, CRP: C-Reactive Protein, RR: Respiratory Rate.

The frequency of various indications for clindamycin use is presented in Table 3. The rates of appropriate indications based on infection type, as well as the causes of inappropriate clindamycin administration, are also demonstrated. All cases of clindamycin use were empirical treatment for anaerobic and staphylococcal infections, as well as prophylaxis of surgical site infections. No cases of definitive therapy based on culture results were recorded.

Table 3. Detailed data of clindamycin indications

Clindamycin indications	Documented indications n (%)	Appropriate indications n (%)	Number of causes of inappropriate indications (n)	
			Duplication therapy	No evidence[#]
Lower respiratory tract infections				
Pneumonia	23 (11.1)	3 (13)	16	4
Aspiration pneumonia	51 (24.5)	32 (62.7)	18	1
Empyema	2 (1.0)	1 (10)	1	0
Lung abscess	1 (0.5)	1 (100)	0	0
Skin and soft tissue infections				
Diabetic foot infection	23 (11.1)	20 (87.0)	3	0
Abscess	5 (2.8)	3 (60.0)	2	0
Cellulitis	6 (2.9)	3 (50.0)	3	0
Mastitis	3 (1.4)	2 (66.7)	1	0
Necrotizing soft tissue infection	2 (1.0)	2 (100)	0	0
Decubitus ulcer infection	8 (3.8)	0 (10)	8	0
Surgical site infection	5 (2.4)	2 (40.0)	2	1
Gynecological infections				
Severe pelvic inflammatory diseases	4 (1.9)	4 (100)	0	0
Postpartum endometritis	7 (3.4)	6 (85.7)	1	0
Septicemia	1 (0.5)	0	1	0
Bone and joint infections				
Osteomyelitis	5 (2.4)	4 (80.0)	1	0
Surgical prophylaxis				
Cesarean delivery during labor or after membrane rupture	22 (10.6)	20 (90.2)	2	0
Other	2 (1.0)	0	2	0
Not documented	38 (18.3)	0	19	19
Total	208 (100)	103 (49.5%)	78 (37.5)	25 (12)

[#]No evidence means there is no record to confirm the suspected infection.

Clindamycin dosages were 600 mg three times daily (TDS) in 168 cases (80.8%) and 900 mg TDS in 40 cases (19.2%). Only three patients with aspiration pneumonia received higher dosages (900 mg) than those recommended in the UpToDate® lexidrug™ clindamycin monograph.

The mean duration of clindamycin administration was 9.7 ± 6.1 days (range: 3–53 days). The most frequent instances of prolonged clindamycin use occurred in cases without appropriate indication, aspiration pneumonia, and surgical site infection prophylaxis (Pearson's chi-square, P = 0.009). Prolonged surgical site infection prophylaxis in cesarean sections was the main cause of 80% of inappropriate clindamycin administration in gynecological cases, with a mean duration of 3.8 ± 1 days (range: 2–6 days).

When considering all three criteria—indication, dose, and duration—and excluding cases with uncertain clindamycin indications or those concurrently receiving other anti-anaerobic or anti-MRSA agents (such as meropenem, imipenem, piperacillin-tazobactam, and vancomycin), 25.5% (53 patients) fully adhered to evidence-based recommendations (Figure 1). Table 4 shows a comparison of study outcomes between appropriate and inappropriate cases of clindamycin use.

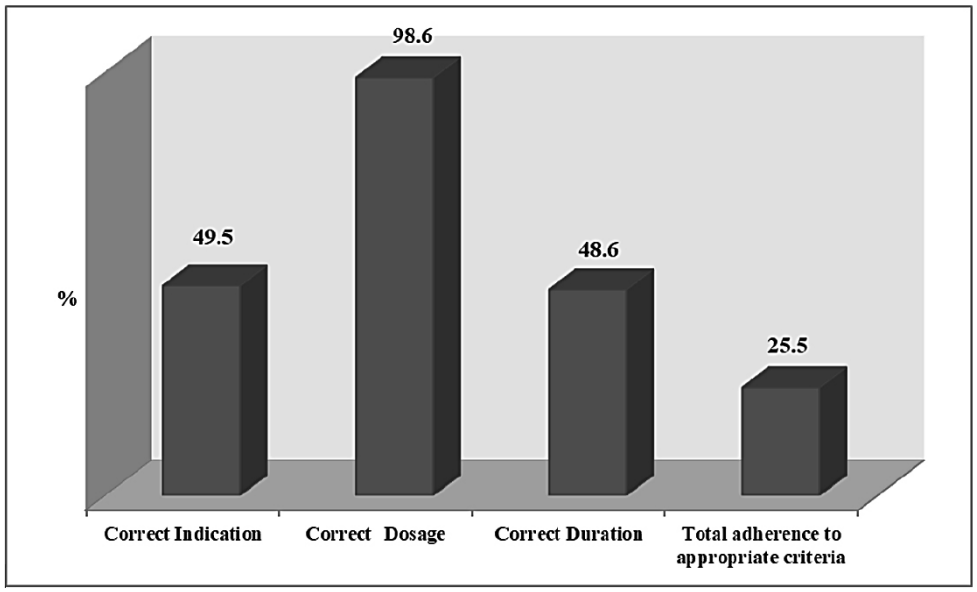

Figure 1. Frequency of appropriate intravenous clindamycin use

Table 4. Comparison of study outcomes between appropriate and inappropriate cases of clindamycin use

Variables	Appropriate use (53)	Inappropriate use (155)	P value
Dose of clindamycin (n)			
600 mg Q 8 hours	43	125	1.000*
900 mg q 8 hours	10	30	
Duration of clindamycin use (mean ± SD)	8.5 ± 3.8	10.1 ± 6.7	0.037
Prescribers n (%)			
Internal medicine specialist	19 (17.1)	92 (82.9)	
Gynecologist	7 (20)	28 (80)	
Cardiologist	1 (25)	3 (75)	
Neurologist	5 (31.3)	11 (69.7)	0.002#
General Surgeon	3 (37.5)	5 (62.5)	
Infectious Disease Specialist	18 (52.9)	16 (47.1)	
Length of hospital stay (days, mean ± SD)	10.8 ± 7.5	12.4 ± 7.9	0.190
Mortality rate (n)	6	36	0.075*

*Fisher's exact test, #Pearson's chi-square.

Figure 2 shows the antibiotics prescribed alongside clindamycin. A total of 54 patients received one additional antibiotic, 81 received two, 56 received three, and 17 received four or more. The most commonly co-administered antibiotics were meropenem and vancomycin.

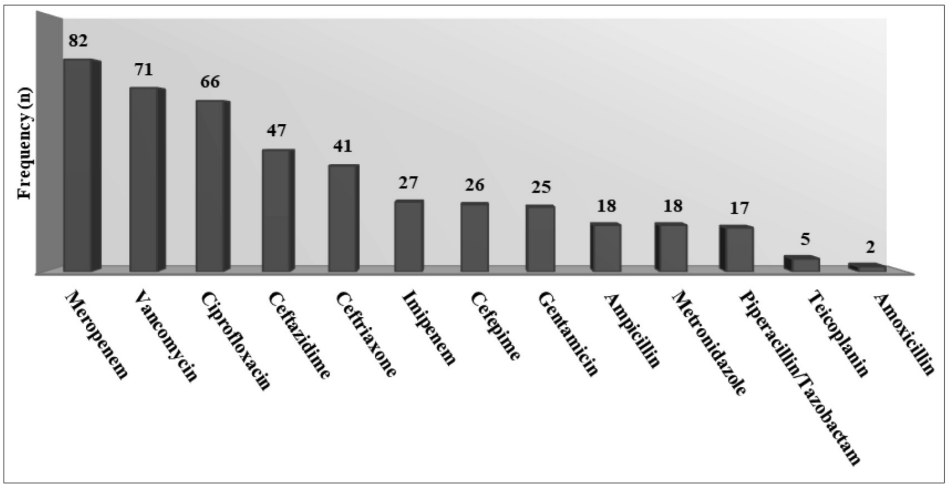

Figure 2. Number of antibiotics co-administered with clindamycin

Figure 3 presents the adherence rates of attending physicians, with the infectious disease specialist demonstrating the highest compliance with prescribing guidelines in most cases involving diabetic foot infections (Pearson's chi-square, P = 0.002).

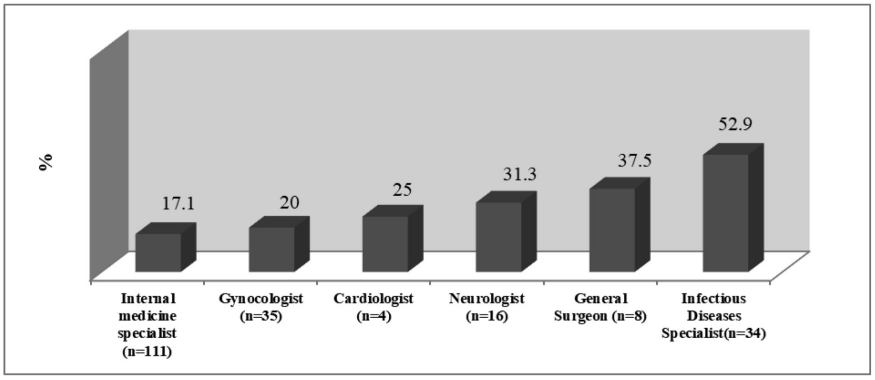

Figure 3. Rate of appropriate clindamycin use according to attending physicians (Pearson's chi-square test: P = 0.002)

Cultures were obtained at admission from 87 patients, yielding a total of 38 positive cultures out of 319 samples collected from various sites, including urine, blood, and sputum. The identified pathogens included Candida albicans, non-albicans Candida species, and Escherichia coli. No bacteria sensitive to clindamycin were detected. One blood culture revealed an Enterobacter strain resistant to carbapenems and aminoglycosides but sensitive to fluoroquinolones. Additionally, meropenem-resistant Pseudomonas aeruginosa was identified in one sputum culture.

Hospital-acquired infections (HAIs) occurred in 19% of patients (40 out of 208). These infections included urinary tract infections (26 cases, 66.7%), central line-associated bloodstream infections (5 cases, 12.8%), ventilator-associated pneumonia (3 cases, 7.7%), and surgical site infections (1 case, 2.6%). Infections developed on average 5.6 ± 3.6 days after admission. Among patients who received clindamycin without a clear indication, 25% developed HAIs. Notably, one case of Staphylococcus aureus bacteremia resistant to both clindamycin and linezolid was identified.

Adverse events were reported in four patients (1.9%), including diarrhea in two patients, generalized skin rash in one patient, and nausea in one patient.

Furthermore, the mean length of hospital stay was 12 ± 7.9 days, and the mortality rate was 20% (42 patients). The rate of inappropriate clindamycin use was significantly higher among patients who did not survive (24.8% [36/145] vs. 9.5% [6/63], P = 0.014). A higher mortality rate was

observed in cases of aspiration pneumonia (n = 16) and in patients without a definitive infection type (n = 13). The average length of hospital stay was significantly longer for non-survivors than for survivors (14.3 ± 8.8 days vs. 11.4 ± 7.5 days, P = 0.036). Additionally, the average age of non-survivors was 71.6 ± 14.1 years, compared to 55.9 ± 19.6 years for survivors (P < 0.001).

Discussion

The findings of this study reveal that intravenous clindamycin was used appropriately in only 25.5% of patients. The primary reasons for its inappropriate use were unconfirmed indications, prolonged treatment duration, and use for surgical prophylaxis. Clindamycin administration was evaluated not only based on its intended indications but also by evaluating its unnecessary use in combination with other antibiotics. For example, if clindamycin was empirically prescribed to a patient already receiving another anti-anaerobic or anti-MRSA antibiotic—except in specific circumstances such as necrotizing fasciitis or toxic shock syndrome— it was considered an inappropriate indication. This approach distinguishes this study from earlier research on clindamycin utilization, which reported a lower rate of irrational clindamycin use (42.9%, mostly due to incorrect dosing and selection) (23,24). An Iranian clindamycin stewardship study found that 61% of its use in hospitals was inappropriate, with pneumonia being the most common off-label indication (5). However, indications were correct in 96% of cases, dosing was appropriate in 47.5%, and duration was appropriate in 35.7%.

In this study, the most common inappropriate use of clindamycin was observed in cases of aspiration pneumonia. Non-severe anaerobic infections are among the indications for clindamycin use. However, it is not recommended as first-line therapy for severe infections due to its bacteriostatic nature, especially when compared to bactericidal agents such as β-lactams or metronidazole (12). Additionally, clindamycin is less effective against beta-lactamase-producing anaerobes than meropenem, tazobactam, and imipenem (25). Furthermore, guidelines recommend against routine anaerobic coverage with clindamycin for suspected aspiration pneumonia unless there is evidence of lung abscess or empyema (26-29). In patients at risk of aspiration, bronchoalveolar lavage revealed gram-negative pathogens in 49% of cases and anaerobes in only 16% (30). While anaerobes may respond better to clindamycin in lung abscesses, current evidence does not support its routine use in aspiration pneumonia (31,32).

Data from randomized controlled trials indicate that both clindamycin and carbapenems are associated with a higher incidence of Clostridium difficile infections (CDIs) compared to other antibiotics. Notably, clindamycin has been linked to more CDI episodes than cephalosporins and penicillins (33). It is important to highlight that ASPs have been shown to reduce the incidence of CDIs by limiting the use of high-risk antibiotics (4,34). For instance, implementing a successful ASP to avoid unnecessary double anaerobic coverage—such as using metronidazole or clindamycin alongside a β-lactam or β-lactamase inhibitor, cephamycin, carbapenem, or moxifloxacin—resulted in a significant 73.9% decrease in inappropriate antibiotic prescriptions (35).

Rational antibiotic use depends on several factors, including selecting the appropriate drug, administering the correct dose, adjusting for renal function, and de-escalating or transitioning to oral therapy when possible (36). The high prevalence of irrational antibiotic prescribing in Iran has been attributed to prescribers' limited professional competence, inadequate informational and functional resources, ineffective supervision, and an inappropriate setting for ASP (37,38).

A large Iranian study demonstrated that implementing the National Antimicrobial Stewardship Program (NASP) reduced antimicrobial use by 23.61%, particularly for imipenem, linezolid, and vancomycin (39). Additionally, the cost of antimicrobial consumption decreased without increasing either the length of hospital stay or the mortality rate. Although clindamycin was not included in the NASP list, its consumption was evaluated as an alternative agent. The antimicrobial consumption index for clindamycin did not change significantly, with defined daily doses reported as 50.3 before the study and 56.5 afterward (P = 0.059).

The antimicrobial time-out approach aims to minimize inappropriate antimicrobial exposure by re-evaluating the prescribed regimen after a specified period, typically on the third day of treatment. This allows clinicians to assess clinical improvement and identify pathogens or causative agents (40). Additionally, this strategy can significantly impact the appropriate prophylactic duration of clindamycin administration for 24 hours following cesarean sections at our medical center.

In the NASP method, an infectious disease specialist reviews the clinical and microbiological evidence of patients within 72 hours to determine whether the prescribing practices are appropriate. A clinical pharmacist then makes the final assessment to adjust the dosage, manage drug interactions, and determine the duration of the antimicrobial agents approved for continuation. Additionally, the clinical pharmacist is responsible for preventing unnecessary duplication of therapy, particularly with anti-anaerobic antibiotics.

The duration of clindamycin treatment was significantly longer in cases involving inappropriate use. Although clindamycin can be prescribed for up to six weeks or longer for certain infections (41), prolonged therapy may increase the risk of Clostridioides difficile infection (CDI), a serious complication associated with clindamycin use (34,42,43). While CDI was not specifically monitored in this study due to its retrospective design, the high rate of irrational use suggests a significant potential risk. Antibiotic stewardship interventions aimed at reducing the use of antibiotics associated with a high risk of CDI are strongly recommended (44). Possible strategies include implementing antibiotic time-outs and stop orders for surgical site infection prophylaxis, encouraging prescribers to routinely review antibiotic regimens to improve prescribing practices.

Limitations

This study had several limitations due to its retrospective design and reliance on archived hospital records, which may be incomplete or inconsistently documented. The absence of microbiological confirmation in more than half of the patients and the lack of severity of illness scores represent additional significant limitations. Furthermore, the absence of post-discharge follow-up restricted our ability to assess long-term adverse effects, including the incidence of CDI or pseudomembranous colitis. Additionally, selecting patients who received intravenous clindamycin for more than 48 hours may have excluded those who were appropriately prescribed short-course prophylaxis for surgical site infections, potentially underestimating appropriate prescribing practices. The small sample size and single-institution setting further limit the generalizability of the results and conclusions.

Conclusion

This study identified a high rate of inappropriate clindamycin use compared to standard regimens, primarily due to unconfirmed infection types, prolonged treatment durations, and unnecessary antibiotic combinations. To promote rational clindamycin use, healthcare providers should adhere to evidence-based guidelines and participate in ongoing education, interdisciplinary collaboration, and specialist involvement. Additionally, the study highlights the need for an Antimicrobial Stewardship Program targeting anti-anaerobic antibiotics in Iran to address medication misuse and reduce the risk of complications. Given the global rise in antibiotic resistance and CDI, increasing awareness among healthcare professionals about rational prescribing practices is essential.

Conflict of Interest

The authors have no relevant financial or non-financial interests to disclose.

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