Original Article

Clindamycin Stewardship: An Opportunity for Hospitalized Patients in Razi Hospital, Rasht, Iran

Abstract

Background: In hospitalized patients, the most common used drugs are antibiotics. Programs designed to rational use of antibiotics improve the quality of care and infection management, and reduce costs. **Aims and Objectives:** The objective of this study was to assess the rational use of clindamycin in Razi Hospital, Rasht, Iran. **Materials and Methods:** This retrospective cross-sectional study was performed in Razi Hospital, Rasht, Iran. All hospitalized patients who received clindamycin were included. Patient's demographic, duration of use and dose of clindamycin therapy, and other concomitant antibiotics were collected from patients' medical records. Rational clindamycin prescribing was evaluated based on recommendations of UpToDate software, version 21.6, Waltham, MA, United States. Analysis of data was performed by the Statistical Package for the Social Sciences software, version 16.0. **Results:** A total of 607 patients receiving clindamycin during 15 months of study were evaluated. The mean age of the patients was 51.51 ± 15.92 years (range: 16–87 years). The most hospitalized patients receiving clindamycin were in internal ward (86%). The most frequently coadministered antibiotics with clindamycin were third-generation cephalosporins (47.9%). The majority of patients admitted in the winter (40.4%). The most frequently primary and final diagnosis in patients receiving clindamycin was reported pneumonia, respectively, 33.1% and 32.1%. Indication, dose, and duration of clindamycin were appropriate in 583 (96%), 277(47.5%), and 208 (35.7%) patients, respectively. **Conclusion:** The rate of incorrect dose and duration of clindamycin in our hospital were significantly high. Also, the majority of its prescription were as off-label indications. Programs for more justified administration of clindamycin to improve quality of care and decrease antibacterial resistance and cost are necessary.

Keywords: *Antibiotic, clindamycin, drug utilization evaluation*

Key message: *Drug utilization evaluation (DUE) is a helpful instrument for evaluation of the rational use of different medications. Programs for more justified administration of antibiotics such as clindamycin to improve quality of care and decrease antibacterial resistance and cost are necessary.*

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Introduction

In hospitalized patients, the most common used drugs are antibiotics. Programs designed to rational use of antibiotics improve the quality of care and infection management, and reduce costs.[1,2] An important problem of health system is enhancement of antimicrobial resistance that influences on outcome and treatment of patients.[3] In over 50% of hospitalized patients, treatment or prophylaxis with antibiotics has been reported incorrectly.[4] Many factors play an important role in the rational use of antibiotics, including proper drug selection, appropriate dosage, dose adjustment based on renal function, and change from the intravenous (IV) administration to oral route.[5]

Different approaches have been proposed to improve the administration of antibiotics and their rational use in hospitalized patients.[6] Drug utilization evaluation (DUE) is a helpful instrument for evaluation of the rational use of different medications.[7]

DUE studies monitor and evaluate the drug prescriptions and help to appropriate use and cost-effectiveness of medications by modifying in prescribing patterns.[8] These studies assess the correct drug use based on predetermined standards and guidelines.[9]

Clindamycin is effective against both gram-positive *cocci* and gram-positive or gram-negative anaerobes. Clindamycin indications include bone and soft tissue, head and neck, respiratory, abdominal, and pelvic infections.[10]

Rate of resistance to the clindamycin was high among strains of *Streptococcus* pneumonia

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that were penicillin-resistant in North America.[11] Also, resistance to clindamycin among anaerobic pathogens has increased from 3% in 1987 to 26% in 2000.[12]

The lack of coordination in prescribing of drugs by physicians in our country is a serious matter, and precise policy on prescribing antibiotics is necessary. However, widespread knowledge of the patterns of consumption and administration of antibiotics in hospitals as a basis is important. To the best of our knowledge, there is not any DUE study conducted in Rasht city, Gilan Province, North of Iran. Due to the lack of information about clindamycin prescription in Razi Hospital, this study aimed to evaluate the rational use of clindamycin in this hospital.

Materials and Methods

This study was a retrospective cross-sectional study carried out in Razi General Hospital Rasht during 15 months. This study was approved by the Research Committee of the Mazandaran University of Medical Sciences, Sari, Iran (Protocol no. IR.MAZUMS.REC.1394.1811). All patients admitted to the Razi Hospital who had received clindamycin were included. Patient's demographic (including age, sex, hospitalization ward, primary, and final diagnosis), route of administration, dose and duration of treatment, cultures, antibiograms, and other concomitant antibiotics were collected in a questionnaire according to the patients' medical records. The appropriateness of clindamycin usage (including dose and duration of use) was assessed based on the indication that was defined in UpToDate software, version 21.6.[13]

Statistical Analysis

The collected data were analyzed by the Statistical Package for the Social Sciences software, version 16.0. Qualitative variables were reported as numbers and percentages, and quantitative variables were reported as mean ± standard deviation (SD). Continuous and qualitative variables between two genders were compared using student's *t*-test and chi-squared test, respectively. The statistical significance level was considered less than 0.05.

Results

A total of 607 patients receiving clindamycin were evaluated. Among them, 356 (58.6%) and 251 cases (41.4%) were man and woman, respectively. The mean age of the patients was 51.51 ± 15.92 years (range: 16–87 years). The mean hospitalization day of the patients was 9.07 ± 6.73 day. The majority of physicians (420 cases [69.2%]) were internist physicians. The most hospitalized patients receiving clindamycin were in internal ward (522 patients [86%]). The highest and lowest seasons of admission were winter (40.4%) and summer (11%), respectively. Among patients, 323 (53.2%), 84 (13.8%), and 43 (7.1%) patients had history of diabetes, surgery, and malignancy, respectively. In terms of receiving other antibiotics except clindamycin, the patients received third-generation cephalosporins, imipenem/meropenem, vancomycin, and metronidazole 291 (47.9%), 92 (15.2%), 28 (4.6%), and 23 (3.8%), respectively. Demographic and clinical data of patients based on gender are shown in Table 1. Of 607 patients, 509 (83.9%) patients received parenteral form of clindamycin and 98 (16.1%) patients received oral clindamycin. In other words, the majority of patients received a clindamycin injection form. The lowest and highest durations of prescribed parenteral clindamycin were 2 days in 20 patients (3.9%) and 13 days in 28 patients (5.5%), respectively. The mean duration use of parenteral clindamycin was reported 7 days. The course of 3 and 5 days oral clindamycin administration was recorded in 21 (21.4%) and 77 (78.6%) of patients. The mean duration use of oral clindamycin was reported 4.6 days. The highest prevalence of primary and final diagnosis in patients receiving clindamycin was pneumonia in 201 patients (33.1%) and 195 patients (32.1%), respectively. With respect to primary and final diagnosis, there were statistically significant difference between men and women ($P < 0.001$) [Table 2].

Of the total patients, 47 patients (7.7%) received dialysis and 7 (1.2%) of the clindamycin-treated patients died.

Indication, dose, and duration of clindamycin were appropriate in 583 (96%), 277 (47.5%), and 208 (35.7%) patients, respectively. The incorrect indications of clindamycin in our study were the urinary tract infection (UTI) and gastrointestinal bleeding. With respect to indication of clindamycin based on labeled and off-label uses, 227 (39%) patients received clindamycin based on labeled use and 356 (61%) patients received based on off-label use. Doses of oral and parenteral clindamycin in different labeled and off-label indications are shown in Table 3. More than half of the patients received low dose and low duration of treatment [Table 4].

Discussion

This study was the first retrospective cross-sectional study that evaluates the rate of appropriate use of clindamycin in Razi Hospital, Rasht.

The main findings of our study were as follows. First, 86% of patients received clindamycin in the internal ward. The reason is that most of patients with multiple diseases and diverse diagnoses are admitted to the internal ward. The most common season of hospitalization of patients was winter and the least prevalent admission season was summer. The most primary and final diagnosis in patients receiving clindamycin was reported pneumonia. Clindamycin is a drug of choice for treatment of aspiration pneumonia and anaerobic necrotizing pneumonia.[10]

In Razi Hospital, injection was the most commonly used route to administration of clindamycin (83.9%). The most commonly antibiotics used with clindamycin in our study were third-generation cephalosporins and carbapenems such as imipenem/meropenem.

Indication, dose, and duration of clindamycin were appropriate in 583 (96%), 277 (47.5%), and 208 (35.7%) patients, respectively.

Table 1: Demographic and clinical data of patients based on gender

Variable		Mean (SD (or number (%)		*P* value
		Man	Woman	
Age (years)		50.7 (17.4)	52.7 (13.6)	0.13
Length of hospitalization (days)		8.7 (6.3)	9.7 (7.3)	0.07
Duration of parenteral clindamycin (days)		6.9 (3.1)	7.4 (3.1)	0.049
Duration of oral clindamycin (days)		4.9 (0.5)	4.3 (0.9)	0.001
Baseline serum creatinine level (mg/dL)		1.2 (0.6)	2.3 (2.6)	<0.001
Other antibiotics used				<0.001
Third-generation cephalosporins		172 (69.6)	119 (63.6)	
Imipenem/meropenem		27 (10.9)	65 (34.7)	
Vancomycin		25 (10.1)	3 (1.6)	
Metronidazole		23 (9.3)	0 (0)	
Physicians	Internal	50.6 (180)	95.6 (240)	<0.001
	Surgery	16.6 (59)	0.4 (1)	
	Infectious	32.9 (117)	4 (10)	
Wards	Internal	79.2 (282)	95.6 (240)	<0.001
	Surgery	8.1 (29)	0.4 (1)	
	Infectious	12.6 (45)	4 (10)	
Seasons of admission	Spring	17.4 (62)	12.4 (31)	<0.001
	Summer	14 (50)	6.8 (17)	
	Fall	36.2 (129)	29.1 (73)	
	Winter	32.3 (115)	51.8 (130)	

Table 2: Frequency of primary and final diagnosis in men and women

Diagnosis		Number (%)		*P* value
		Man	Woman	
Primary	Osteomyelitis	19.7 (70)	18.3 (46)	<0.001
	Pneumonia	27.2 (97)	41.4 (104)	
	Preoperative prophylaxis	0.6 (2)	0 (0)	
	UTI	93.9 (14)	0.8 (2)	
	Cellulitis	2.8 (10)	0 (0)	
	Arthritis	0 (0)	8 (20)	
	Gastrointestinal bleeding	1.1 (4)	0 (0)	
	Device-associated infection	2.2 (8)	0 (0)	
	Lung abscess	6.7 (24)	7.2 (18)	
	Diabetic foot	35.7 (127)	24.3 (61)	
Final	Osteomyelitis	21.3 (76)	14.7 (37)	<0.001
	Pneumonia	28.4 (101)	37.5 (94)	
	UTI	4.2 (15)	1.2 (3)	
	Gastrointestinal bleeding	1.7 (6)	0 (0)	
	Arthritis	1.7 (6)	6.8 (17)	
	Lung abscess	15.7 (56)	13.9 (35)	
	Diabetic foot	27 (96)	25.9 (65)	

UTI = urinary tract infection

Clindamycin is FDA-approved (Food and Drug Adminstration) for the treatment of septicemia, intraabdominal infections, lower respiratory infections, gynecological infections, bone and joint infections, and skin and skin structure infections.[10] Unfortunately, in our study clindamycin was prescribed in 24 patients for incorrect indications (UTI and gastrointestinal bleeding). In our study, the majority of indications for clindamycin administration (61%) were off-label. Antibiotics are the most prescribed medication as off-label among patients. Clinicians should only use off-label drugs in patients when there are no effective alternatives are available.[14] A cross-sectional study conducted to describe the off-label use of antibacterial in prescriptions for hospitalized adult patients. They found that about one-third of the antibacterial was prescribed for off-label use.[15] In our study, the majority of clindamycin prescription were off-label. Because of the dramatic scenario of increased antibacterial resistance, it is necessary to prescribe antibiotics for approved uses.

Table 3: Doses of oral and parenteral clindamycin in different label and off-label indications

Indication	Oral clindamycin Dose (number of patients)	Parenteral clindamycin Dose (number of patients)
Osteomyelitis	150 mg q6h (21)	300 mg q12h (16)
	300 mg q6h (17)	300 mg q8h (29)
		600 mg q8h (30)
Pneumonia	150 mg q6h (25)	300 mg q8h (47)
	300 mg q6h (17)	600 mg q12h (16)
		600 mg q8h (90)
Arthritis	–	300 mg q8h (3)
		600 mg q8h (20)
Lung abscess	–	300 mg q12h (20)
	–	300 mg q8h (16)
	–	600 mg q8h (55)
Diabetic foot	–	300 mg q8h (79)
		600 mg q8h (82)

Table 4: Clindamycin use based on recommendations of UpToDate 21.6 (*n* = 607)

Variable	Number (%)	
	Appropriate	Inappropriate
Indication	583 (96)	24 (4)
Dose	277 (47.5)	306 (52.5)
Duration	208 (35.7)	375 (64.3)

More than half of the patients received low dose and duration of treatment. The low doses of antibiotics cause microbial resistance and the infection does not improve. On the contrary, duration of hospitalization, mortality, and costs increase.

In many studies, the inappropriate use of antibiotics was determined in Iranian population.[7,16-18] The previous retrospective study for evaluation of clinical use of clindamycin found that the use of it was consistent with its indications. However, high dose, incorrect time of preventive medication, and long-time use of clindamycin were reported. Clindamycin was most commonly used in the surgical ward in their study.[19] In contrast to this study, we observed low dose and low duration of clindamycin use in our hospital. One explanation of this difference is related to different guidelines used for assessing clindamycin use.

To the best of our knowledge, there is not any study in Iranian population similar to ours evaluating clindamycin use in hospital setting.

In Alavi *et al.*'s[17] study, clindamycin was the third most commonly used drug in Razi Hospital, Ahvaz.

In a study to assess the antibiotic use in a teaching hospital, only two prescriptions were related to clindamycin. They reported that this antibiotic in terms of dose, frequency, and duration had been used appropriately.[20] Findings of this study were not comparable to our study because of small number of cases.

A therapeutic drug monitoring (TDM) program for evaluation the usage of parenteral clindamycin showed that 22.4% of patients did not meet the criteria.[21] In our study, in 503 of 509 patients (99%) the use of parenteral clindamycin was appropriate. Our findings showed that the appropriate use of clindamycin was higher than Gin *et al.*'s[21] study.

Clindamycin is one of the antibiotics that causes clostridium difficile-associated disease (CDAD), which is the most important cause of nosocomial diarrhea in industrialized countries.[22] Decrease in CDAD by restricting the use of clindamycin has been reported successfully.[23] Because of this side effect, it is best to restrict use it to the specific patients (patients with severe allergy to β-lactams, streptococcal toxic shock syndrome, or necrotizing infections).[22]

In Hajebi *et al.*'s[24] study, clindamycin was the fifth costly antibiotic in Taleghani Hospital, Tehran. The cost of parenteral clindamycin is significantly high.[25] The cost-effectiveness of oral clindamycin showed in previous study.[26] The oral absorption of clindamycin has been reported well.[27] In our setting, the administration of IV form of clindamycin was high. Therefore, it is advisable to physicians to change the injectable form to oral according to clinical conditions of patients.

Usual parenteral doses are 600 mg every 6–8 h to 900 mg every 8 h. Typical oral doses are 150–450 mg every 6 h.[10] Regardless of the indications of clindamycin, range of clindamycin dose used in our study was consistent with stated range of dose.

Pharmacokinetic data of clindamycin suggested the potential use of 1200 mg of clindamycin every 12 h instead of 600 mg every 6 h.[28] Clindamycin at dosage of 300 mg IV or oral every 8h or every 12h is effective adequately against *Staphylococcus aureus*, *Streptococcus pneumonia*, and *Bacteroides fragilis*.[29] *In vitro* model, the antibacterial activity of clindamycin at 300 mg every 12 h was equivalent to 300 or 600 mg every 8 h.[30] Change in clindamycin dosing from 600 mg every 6 h to 600 mg every 8 h showed no differences in clinical outcomes. Furthermore, the mean febrile days and antibiotic-associated adverse effect statistically significant decreased.[31]

The physicians in our hospital in over half of cases administered lower dose and lower duration of clindamycin treatment than recommendations of UpToDate software, version 21.6. However, we should not forget that the low dose of treatment is as effective as high dose. Therefore, it is necessary for physicians to pay attention to clinical conditions of patients and follow the guidelines for rational use of clindamycin.

To the best of our knowledge, there are not sufficient studies similar to ours evaluating clindamycin use in hospital setting. It should be noted that definitions of appropriate use are different in the literature.[4] In this study, we evaluate clindamycin consumption according to recommendations of UpToDate software, version 21.6 that different from other studies. One of the most used methods for DUE is anatomical therapeutic chemical (ATC) classification system.[32]

One of the advantages of this study is the comparison of clindamycin use in different seasons. We observed that the most admission of patients was in winter. It may be related to the high rate of infectious diseases (especially pneumonia) in the cold seasons of the year. Other advantage of this study was a large sample size (607 patients). Due to the lack of records and attention to the registration of drug side effects by the relevant medical staff, no adverse effects were recorded in these cases.

Some of our study limitations are as follows: The first concerns the reference for appropriate use of the clindamycin in our hospital. Second, appropriateness was evaluated retrospectively based on patient's files and some data may not be recorded. Third, this study was conducted in one teaching hospital in Rasht, Iran.

Extensive education about the correct use of antibiotics in clinical practice remains necessary. The findings of our study may be useful for physicians to improve the selection of clindamycin individually and reduce the cost of treatment. Selection of antibiotic or change it based on laboratory results (culture and antibiogram) and consultation with an infectious specialists are the safest ways to rational prescribe of antibiotics.

Further study is needed to estimate the rate of usage for clindamycin among other antibiotics based on ATC (Anatomical Therapeutic Chemical) classification in Razi Hospital, Rasht.

Conclusion

In our center, the majority of use of clindamycin is in line with its indications (96%), but the majority of its prescription were as off-label. Because of the dramatic scenario of increased antibacterial resistance, it is necessary to prescribe antibiotics for approved uses. Also, more than half of the patients received low dose and duration of treatment. The rate of incorrect dose and duration of clindamycin in our hospital was significantly high. Programs for more justified administration of clindamycin to improve quality of care and decrease antibacterial resistance and cost are necessary.

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Conflicts of interest

There are no conflicts of interest.

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