CASE REPORT

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A Rare Side Effect of Ciprofloxacin: Venous Thrombophlebitis

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ABSTRACT Quinolone antibiotics are commonly prescribed for a range of infections because of their broad-spectrum effectiveness, especially against gram-negative bacteria. The quinolones can be classified into four generations based on antimicrobial activity. Third-generation quinolones offer extended activity against gram-negative and atypical intracellular bacteria and provide improved coverage against gram-positive bacteria, unlike the first and second generations. Ciprofloxacin, a third-generation quinolone as antibacterial medication, is known for its potent bactericidal effects, wide spectrum of antibacterial activity, high permeability, and minimal side effects. Common adverse reactions include abdominal pain, diarrhea, dizziness, headaches, and insomnia. We review a case of an erythematous rash that appeared to be superficial venous thrombophlebitis 5 minutes after infusion of ciprofloxacin.

Keywords: Adverse effects; ciprofloxacin; thrombophlebitis

Ciprofloxacin is a third generation quinolone which is characterized by its strong bactericidal power, broad antibacterial spectrum, high-permeability and low side effects. The most common adverse effects include abdominal pain, diarrhea, dizziness, headache and insomnia.[1-3]

Many antibiotics are administered intravenously (IV) to show rapid and high efficacy against pathogenic microorganisms. Although administration of drugs via IV route is preferred to ensure effective blood concentration and rapid onset of action, it may cause complications related to administration such as thrombophlebitis.[4,5] The factors causing thrombophlebitis development can be listed as the solvent in which the drug is diluted, pH, osmolarity, amount of drug used, infusion rate and vesicant properties of antimicrobial drugs. Borgonovo et al. 2023 systematically reviewed randomized controlled trials and made recommendations by determining the solvent, pH, osmolarity, amount of drug administered, infusion rate, vesicant properties and thrombophlebitis rate of commonly used antimicrobial drugs. Also pH for ciprofloxacin; 3.3-4.6, the incidence of phlebitis was reported to be ≥5 with vesicant properties, 9% NaCl /D5W was used as diluent, dosage was 400 mg every 8-12 hours, infusion rate was reported to be more than 60 minutes. The chemical properties of the drugs were analyzed and 37 antibiotics including ciprofloxacin were found to have osmolarity >600 mOsm/L, pH<5 or >9, and it was stated that these

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drugs should be used with caution because they have a high incidence of phlebitis such as vesican-containing drugs.[4] In this study, a rare case of venous thrombophlebitis associated with commonly prescribed ciprofloxacin was presented.

CASE REPORT

An 85-year-old woman was hospitalized to the neurosurgery service for surgery with a diagnosis of L4-L5 listhesis. The patient, whose preoperative preparations were ongoing, had watery diarrhea and nausea 4-5 times starting 1 day before the operation. However, there was no fever and vomiting. In detailed anamnesis, stool microscopy and culture, complete urine and urine culture were requested from the patient who complained of right flank pain and dysuria. The urine culture yield *Escherichia coli* and IV ciprofloxacin treatment was started. The patient, who had no previous history of drug allergy and had used oral ciprofloxacin many times, developed redness along the vascular trace, which started approximately 5 minutes after IV ciprofloxacin administration and rapidly increased within 30-60 second and became prominent, appearing like superficial venous thrombophlebitis (Figure 1). The patient had no itching but complained of mild pain. The patient's treatment was stopped immediately. Although it may be assumed to be an allergic reaction due to the suddenness of the reaction, no systemic complications were observed. Local erythema and pain resolved within a few hours after discontinuation of IV ciprofloxacin.

Informed consent was obtained from the patient.

FIGURE 1: Vascular tracing image of the patient at 5 minutes after intravenous ciprofloxacin administration.

DISCUSSION

The appropriate type of vascular access device (VAD) is determined depending on the recommended treatment, duration, patient characteristics and the health center where the treatment is administered.[6] The chemical properties of the drugs have a significant effect on the choice of VAD. The leads of central vascular access devices are inserted into large-caliber vessels, which guarantees the ability to inject all types of solutions. Moreover, peripheral vascular access devices (PVAD) are incompatible with certain medications, including those with low pH (<5) or high pH (>9), medications with high osmolarity (>600 mOsm/L), and vesicant drugs. The leakage of these substances through the vessel lumen could result in potential tissue damage.[7]

Peripheral vessels are a slow-flow system. Administering an irritating drug through the PVAD can lead to thrombosis by damaging the endothelial membrane of the intimal layer, potentially triggering inflammatory processes involving the tunica media. This can result in edema, infiltration, and severe injury extending to the vessel wall. The events defined thus far represents the pathologic correlates of thrombophlebitis.[4,8,9]

Extreme caution is required during administration of drugs. In this subgroup of antimicrobials, it is important to choose the right VAD to avoid

complications related to peripheral IV administration. A comprehensive grasp of the physicochemical properties of antimicrobials is imperative for significantly bolstering patient safety and consequently averting misapplication and adverse local effects.

Ensuring safe treatment is the cornerstone of pharmacologic therapy. VAD failure, attributed to complications such as inflammatory events or infusion leakage through the venous wall, can lead to substantial issues: tissue damage, treatment delivery delays, heightened costs, prolonged hospital stays, or even compensation claims.[10,11]

The utilization of peripheral catheters for IV treatment administration is a widely employed strategy worldwide. Nevertheless, although it has clear benefits (cost control, ease of use and basic management), this access has a significant number of complications.[9]

For instance, a meta-analysis carried out in 2019 encompassing 35 studies (involving over 15,000 patients) revealed a phlebitis incidence rate of 30.7 per 100 catheters. According to this study, prolonged hospitalization, antibiotic use, female gender, placement in the forearm, presence of infection, and use of Teflon cannula were the primary risk factors for phlebitis. Therefore, solving this problem requires a multifaceted approach. Several considerations come into play, including the general health status of the patient, the quantity and quality of accessible vessels, the selection of appropriate vascular devices, their correct application and the implementation of an effective monitoring system. Furthermore, it is crucial to take into account the chemical properties of the drugs used; pH and osmolarity are recognized as important risk factors.[1,2] Enhancing the safety of IV therapy is crucial and should be a primary focus within healthcare settings. It may be useful to know the pharmacologic properties of drugs to assess the risks of their administration in relation to their physicochemical structure.

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Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: *Sema Güler;* ***Design:*** *Sema Güler;* ***Control/Supervision:*** *Sema Güler;* ***Data Collection and/or Processing:*** *Sema Güler;* ***Analysis and/or Interpretation:*** *Sema Güler;* ***Literature Review:*** *Sinem Pehlivan;* ***Writing the Article:*** *Sinem Pehlivan;* ***Critical Review:*** *Sinem Pehlivan.*

REFERENCES

1. Xue Z, Xiang Y, Li Y, Yang Q. A systematic review and meta-analysis of levofloxacin and ciprofloxacin in the treatment of urinary tract infection. Ann Palliat Med. 2021;10(9):9765-71. [Crossref] [PubMed]
2. Ibrahim NM, Fahim SH, Hassan M, Farag AE, Georgey HH. Design and synthesis of ciprofloxacin-sulfonamide hybrids to manipulate ciprofloxacin pharmacological qualities: potency and side effects. Eur J Med Chem. 2022;228:114021. [Crossref] [PubMed]
3. Kolpen M, Mousavi N, Sams T, Bjarnsholt T, Ciofu O, Moser C, et al. Reinforcement of the bactericidal effect of ciprofloxacin on Pseudomonas aeruginosa biofilm by hyperbaric oxygen treatment. Int J Antimicrob Agents. 2016;47(2):163-7. [Crossref] [PubMed]
4. Borgonovo F, Quici M, Gidaro A, Giustivi D, Cattaneo D, Gervasoni C, et al. Physicochemical characteristics of antimicrobials and practical recommendations for intravenous administration: a systematic review. Antibiotics (Basel). 2023;12(8):1338. [Crossref] [PubMed] [PMC]
5. Ballesteros-Peña S, Fernández-Aedo I, Vallejo-De la Hoz G, Tønnesen J, Miguelez C. Identification of potentially irritating intravenous medications. Enferm Intensiva (Engl Ed). 2022;33(3):132-40. [Crossref] [PubMed]
6. Gorski LA, Hadaway L, Hagle ME, Broadhurst D, Clare S, Kleidon T, et al. Infusion therapy standards of practice, 8th edition. J Infus Nurs. 2021 01;44(1S Suppl 1):S1-S224. [Crossref] [PubMed]
7. Pittiruti M, Van Boxtel T, Scoppettuolo G, Carr P, Konstantinou E, Ortiz Miluy G, et al. European recommendations on the proper indication and use of peripheral venous access devices (the ERPIUP consensus): a WoCoVA project. J Vasc Access. 2023;24(1):165-82. [Crossref] [PubMed]
8. Lewis GBH, Hecker JF. Infusion thrombophlebitis. British Journal of Anaesthesia. 1985;57(2):220-33. [Crossref] [PubMed]
9. Yasuda H, Yamamoto R, Hayashi Y, Kotani Y, Kishihara Y, Kondo N, et al; AMOR-VENUS study group. Occurrence and incidence rate of peripheral intravascular catheter-related phlebitis and complications in critically ill patients: a prospective cohort study (AMOR-VENUS study). J Intensive Care. 2021;9(1):3. [Crossref] [PubMed] [PMC]
10. Helm RE, Klausner JD, Klemperer JD, Flint LM, Huang E. Accepted but unacceptable: peripheral IV catheter failure. J Infus Nurs. 2019;42(3):151-64. [Crossref] [PubMed]
11. Marsh N, Larsen EN, Takashima M, Kleidon T, Keogh S, Ullman AJ, et al. Peripheral intravenous catheter failure: a secondary analysis of risks from 11,830 catheters. Int J Nurs Stud. 2021;124:104095. [Crossref] [PubMed]