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Clinical Audit of Primary Treatment of Open Fractures: Antibiotic Treatment and Tetanus Prophylaxis*

Auditoria clínica do tratamento primário de fraturas expostas: Tratamento antimicrobiano e profilaxia antitetânica

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Abstract

Objective To evaluate whether the conducts involving antimicrobial treatment and prophylaxis against tetanus have been performed according to the Clinical Protocol of the Institution.

Methods Descriptive and retrospective study conducted in patients of both genders, > 18 years old admitted to a public hospital specialized in emergency and trauma, to treat primary open fracture. The data of interest were surveyed in medical records, drug prescriptions, report of patients admitted in the Surgical Block and tetanus prophylaxis requests.

Results A total of 241 patients were selected, mostly male (81.7%), young adults (64.3%), victims of motorcycle accidents (53.5%). Infectious complications were present in 18.7% of the fractures, the mean time for the surgical approach was 4 hours and 12 minutes, and 91.7% of the patients had preoperative antimicrobial prescription. The main inadequacies identified were: period of prescription of antimicrobial treatment (63.5%); choice of the antimicrobial scheme (59.3%) and antimicrobial dose (58.0%). Only 14.1% of the patients were immunized against tetanus.

Conclusion The greatest divergences with the Clinical Protocol were observed in the issues involving the antimicrobial regimen used, doses and time of prescription, as well as in tetanus prophylaxis.

Keywords
- open fracture
- antibiotic prophylaxis
- infection
- tetanus

Resumo

Objetivo Avaliar se as condutas envolvendo o tratamento antimicrobiano e a profilaxia contra o tétano têm sido realizadas conforme o Protocolo Clínico da Instituição.

Métodos Estudo descritivo e retrospectivo, realizado em pacientes de ambos os gêneros, > 18 anos, admitidos em um hospital público estadual especializado em urgência e trauma, para tratamento primário de fratura exposta. Os dados de interesse

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foram pesquisados em prontuários médicos, prescrições de medicamentos, relatórios de pacientes admitidos no Bloco Cirúrgico e solicitações de profilaxia antitetânica.

Resultados Foram selecionados 241 pacientes, a maioria homens (81,7%), adultos jovens (64,3%), vítimas de acidentes motociclísticos (53,5%). As complicações infecciosas estiveram presentes em 18,7% das fraturas, o tempo médio para a abordagem cirúrgica foi de 4 horas e 12 minutos, e 91,7% dos pacientes tiveram prescrição do tratamento antimicrobiano no pré-operatório. As principais inadequações identificadas foram: período de prescrição do tratamento antimicrobiano (63,5%); escolha do esquema de antimicrobianos (59,3%) e dose dos antimicrobianos (58,0%). Apenas 14,1% dos pacientes foram imunizados contra o tétano.

Conclusão As maiores divergências com o Protocolo Clínico foram observadas nas questões envolvendo o esquema de antimicrobianos utilizados, doses e tempo de prescrição, bem como na profilaxia antitetânica.

Palavras-chave
- fraturas expostas
- antibioticoprofilaxia
- infecção
- tétano

Introduction

Open fractures (OFs) are characterized by a communication between the fracture focus and the external environment or contaminated cavities through a soft tissue injury, which favors contamination and impairs healing. As a result, the clinical approach to these fractures is difficult and their prognosis is worse.[1] In major urban centers, OFs are mostly caused by traffic accidents, affecting men from the economically active age group.[2,3]

There are several classifications for OF according to lesion severity and contamination degree, which affects prognosis and therapeutic choices.[1] Gustilo et al[4] propose a system considering trauma energy, soft tissue injury degree and contamination degree to classify OFs as types I, II and III.[1,5] Higher classification levels are associated with greater extent, severity, soft tissue involvement and contamination, and, therefore, higher risk of infections.[6]

An antimicrobial treatment, preferably starting in the first hours after OF occurrence, is advocated to minimize the incidence of infectious complications.[5,7] The intravenous administration of an antibiotic agent has a protective role against infections,[8] and the earlier its institution, the better the outcomes.[9]

The primary treatment of OFs must also include tetanus prophylaxis;[5,9] although this is a life-threatening infectious disease, tetanus is preventable through immunization. Transmission often occurs by the *Clostridium tetani* bacillus introduction in puncturing wounds contaminated with soil, dust, animal or human feces. Clinically, the disease presents with neurotoxic symptoms resulting from the action of the bacillus-produced toxin.[10]

At Fundação Hospitalar do Estado de Minas Gerais (FHEMIG, in the Portuguese acronym), the guidelines for initial OF care are established by the Clinical Protocol (CP) "Primary Treatment of Exposed Fractures" ("Tratamento Primário das Fraturas Expostas"). One of the goals of this Protocol is to reduce the incidence of infections.[11] To do so, several approaches were standardized, including the initial treatment of open fractures with antimicrobial agents and tetanus prophylaxis. Both antimicrobial treatment and tetanus prophylaxis must be used rationally to ensure the efficacy and safety of antibiotic drugs and immunobiological products and to improve resources management in patient care.[12]

However, the mere elaboration and publication of protocols are not enough to ensure proper assistance. Strategies are required to assess adherence to agreed behaviors. One of these strategies is a Clinical Audit (CA), a structured process for clinical practice evaluation according to established guidelines, followed by educational measures and implementation of necessary changes.[13]

Thus, the present study, in the form of a CA, aims to evaluate whether the antimicrobial treatment and tetanus prophylaxis in the initial care of patients with open fracture have been performed according to the guidelines established by the CP adopted by the institution.

Methods

The present CA was performed through a descriptive and retrospective study analyzing the initial consultations for OF surgical treatment from June to December 2016 in a state public hospital specialized in urgency and trauma. Both male and female patients, >18 years old with appendicular skeleton fracture were selected. Patients with hand fractures were excluded because these injuries have their own protocol.

Data were obtained in medical records, medication prescriptions from the Hospital Management System (SIGH, in the Portuguese acronym), reports of patients admitted to the Surgical Department for emergency OF surgery and tetanus prophylaxis requests.

Patients were characterized according to gender, age and origin. The OF was evaluated according to the trauma mechanism, affected limb and the Gustilo classification. Osteomyelitis and soft tissue infection, the infectious complications investigated, were identified through a conclusive medical

diagnosis included in the patient records by physicians from the traumatology team.

The initial antimicrobial treatment was evaluated based on the antimicrobial regimen used, doses, prescribed treatment duration, time elapsed between admission and antimicrobial treatment initiation and waiting time for surgery. These data were compared with CP recommendations detailed in ►**Box 1**.

The indication for tetanus prophylaxis was evaluated according to the vaccination history of the patient detailed at the medical record. In addition, the length of stay for OF initial approach and treatment, as well as the care flow within the hospital network, were investigated.

Frequencies, measures of central tendency and dispersion measures were obtained for statistical analysis. The association between categorical variables was assessed using the Pearson chi-squared test (χ^2) with a 5% significance level ($p < 0.05$). The study was approved by the institutional Research Ethics Committee under the protocol number 2.211.687/2017.

Box 1 Recommendations for antimicrobial treatment and tetanus prophylaxis from the Clinical Protocol "Primary Treatment of Exposed Fractures" - FHEMIG, 2014.

ANTIMICROBIAL AGENTS	RECOMMENDATIONS
Starting time	Treatment must start at the preoperative period
Choice of antimicrobial agents	**Type I fractures**: cefazolin, 1 g IV every 6 hours
	Type II fractures: cefazolin, 1 g IV every 6 hours + gentamycin, 240 mg IV every 24 hours
	Alternative regimen for type I and II fractures: clindamicina 600 mg EV de 6/6 hours + gentamycin, 240 mg IV every 24 hours
	Type III fractures: cefazolin, 1 g IV every 6 hours + gentamycin, 240 mg IV every 24 hours + metronidazole, 500 mg every 6 hours
	For fractures occurring in rural environment and with gross contamination, add metronidazole, 500 mg every 6 hours
Treatment duration	**Type I** and **II**: 24 hours
	Type III: 72 hours
TETANUS PROPHYLAXIS	**RECOMMENDATIONS**
	Evaluate requirement based on the vaccination history of the patient
	In case of doubt regarding previous tetanus prophylaxis: add metronidazole, 500 mg every 6 hours

Adapted from Protocolo Clínico "Tratamento Primário das Fraturas Expostas" – FHEMIG,2014.

Results

During the study period, 241 patients with OF were identified, predominantly male (81.7%), young adults (64.3%), victims of motorcycle accidents (53.5%). Lower limbs were the most affected anatomical segment (82.6%) (►**Table 1**).

According to the Gustilo classification, 48 (20.0%) fractures were type I, 46 (19.0%) were type II, and 52 (21.6%) were type III. This classification was not recorded in medical records of 39.4% patients with OF. After the initial approach,

Table 1 Characterization by gender, age group, origin, trauma mechanism and affected anatomical segment of patients receiving primary treatment for open fractures from June to December 2016, Hospital João XXIII, Belo Horizonte, Minas Gerais, Brazil.

Variables	Patients primarily treated for open fractures ($n = 241$)	
	n	(%)
Gender		
Male	197	81.7
Female	44	18.3
Age group (37.2 ± 16.0 years old; 18–86 years-old)		
18–39 years-old	155	64.3
40–59 years-old	62	25.7
$\geq$ 60 years-old	24	10.0
Origin		
Belo Horizonte Metropolitan Region	192	79.7
Minas Gerais State, except for RMBH	48	19.9
Not informed	1	0.4
Trauma mechanism		
Car accident	15	6.2
Bicycle accident	5	2.1
Machinery accident	10	4.1
Motorcycle accident	129	53.5
Physical assault	5	2.1
Running over	33	13.7
Firearm or knife assault	8	3.3
Fall	32	13.3
Other	4	1.7
Affected anatomical segment		
Lower limb	199	82.6
Upper limb	38	15.8
Lower + upper limbs	4	1.6

Abbreviation: RMBH, Belo Horizonte metropolitan region.

infectious complications occurred in 18.7% patients, most often in those with type III fractures (36.5%).

The average waiting time for emergency surgery was 4 hours and 12 minutes ± 3 hours and 18 minutes, ranging from 38 minutes to 21 hours and 7 minutes; 199 (82.6%) patients were operated on within 6 hours of admission. Preoperative antimicrobial treatment was prescribed for 221 (91.7%) patients; in addition, for 172 subjects (71.7%), antimicrobial treatment was prescribed within 3 hours of admission. There was a statistically significant association between infectious complications and type III fractures ($p = 0.0014$), postoperative antimicrobial treatment ($p = 0.0362$) and antimicrobial treatment starting 3 hours after admission ($p = 0.0350$); these data are presented in ►**Table 2**.

From the total sample of 241 patients, 74 (30.7%) were excluded from the antimicrobial treatment evaluation because of the lack of fracture classification record and the lack of criteria for antimicrobial treatment in type III fractures from trauma cases occurred > 6 hours before.

Inadequacies regarding the choice of antimicrobial regimen, prescribed doses and antimicrobial treatment duration outweighed adequacies, as shown in ►**Figure 1**.

Table 2 Distribution of infectious complications by fracture classification, waiting time for surgery and time between admission and antimicrobial treatment start from June to December 2016, Hospital João XXIII, Belo Horizonte, Minas Gerais, Brazil.

Variables	Patients with open fracture ($n = 241$)		Infectious complications				*p-value**
			YES ($n = 45$)		NO ($n = 196$)		
	n	(%)	*n*	(%)	*n*	(%)	
Open fracture classification							
Type I	048	(20.0)	05	(10.4)	043	(89.6)	$p = 0.0014$
Type II	046	(19.0)	04	(08.7)	042	(91.3)	
Type III	052	(21.6)	19	(36.5)	033	(63.5)	
Unclassified	095	(39.4)	17	(17.9)	078	(82.1)	
Time from patient admission to surgery							
≤ 6 hours	199	(82.6)	37	(18.6)	162	(81.4)	$p = 0.4621$
> 6 hours	042	(17.4)	08	(19.0)	034	(81.0)	
Time from patient admission to antimicrobial treatment start							
Preoperative	221	(91.7)	38	(17.2)	183	(82.8)	$p = 0.0362$
Postoperative	020	(08.3)	07	(35.0)	013	(65.0)	
≤ 3 hours after admission	172	(71.7)	27	(15.7)	145	(84.3)	$p = 0.0350$
> 3 hours after admission	069	(28.3)	18	(26.1)	051	(73.9)	
TOTAL	**241**	**(100)**	**45**	**(18.7)**	**196**	**(81.3)**	

*χ^2 test, significance level $p < 0.05$.

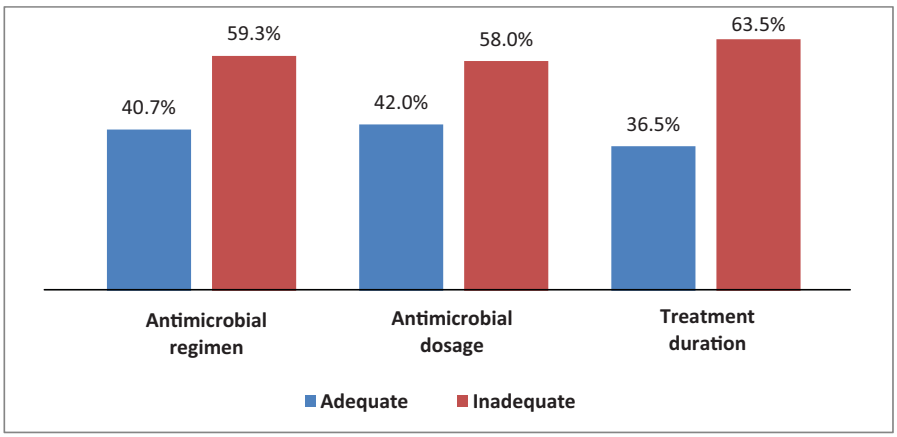

Fig. 1 Distribution of antimicrobial regimens, prescribed doses and treatment duration adequacies and inadequacies according to the Clinical Protocol "Primary Treatment of Exposed Fractures" - FHEMIG guidelines from June to December 2016, Hospital João XXIII, Belo Horizonte, Minas Gerais, Brazil.

Regarding antimicrobial agents, 59.3% of the patients were exposed to associations not recommended by the CP. The highest percentage of inadequacies was observed in patients with type III OFs and/or trauma occurred > 6 hours before (75.0%) and in those with type II OFs (40.0%). The main inadequacies were, respectively, the absence of the metronidazole prescription for anaerobic bacteria coverage (55.5%) and the absence of the gentamicin prescription for extended gram-negative coverage (87.4%) (►**Table 3**).

Considering the total of 438 antimicrobial agents prescribed for the evaluated treatment regimens, daily doses of 254 (58.0%) drugs were inconsistent with the CP. Most inadequacies occurred in prescriptions of cefazolin (93.0%) and clindamycin (86.0%). In contrast, most of the prescribed doses of metronidazole (65.0%) were adequate. All gentamicin dosages agreed with the CP (►**Figure 2**).

As for duration, 63.5% of antimicrobial treatments were prescribed for an inadequate period. Most significant results

Table 3 Description of inadequacies per fracture type and antimicrobial regimens according to the Clinical Protocol "Primary Treatment of Exposed Fractures" - FHEMIG, from June to December 2016, Hospital João XXIII, Belo Horizonte, Minas Gerais, Brazil

ANTIMICROBIAL TREATMENT	Patients ($n = 167$)	
	n	(%)
Type I		
Adequate	20	(645)
Inadequate	11	(35.5)
Trauma occurred in rural environment and/or contamination with dirt with no coverage for anaerobic organisms	03	(27.3)
Increased coverage for gram-negative organisms is unrequired	03	(27.3)
Increased coverage for gram-negative and anaerobic organisms is unrequired	04	(36.3)
Alternative regimen: Clindamycin not associated with gentamycin	01	(09.1)
Type II		
Adequate	24	(60.0)
Inadequate	16	(40.0)
Trauma occurred in rural environment and/or contamination with dirt with no coverage for anaerobic organisms	01	(06.3)
No increased coverage for gram-negative organisms	14	(87.4)
Coverage for anaerobic agents is not required	01	(06.3)
Type III and/or trauma over 6 hours before		
Adequate	24	(25.0)
Inadequate	72	(75.0)
No coverage for gram-negative organisms	40	(55.5)
No increased coverage for gram-negative and anaerobic organisms	21	(29.2)
No increased coverage for gram-negative organisms	06	(08.3)
Use of not recommended antimicrobial agent (ceftriaxone)	05	(06.9)
Adequacies	**68**	**(040.7)**
Inadequacies	**99**	**(059.3)**

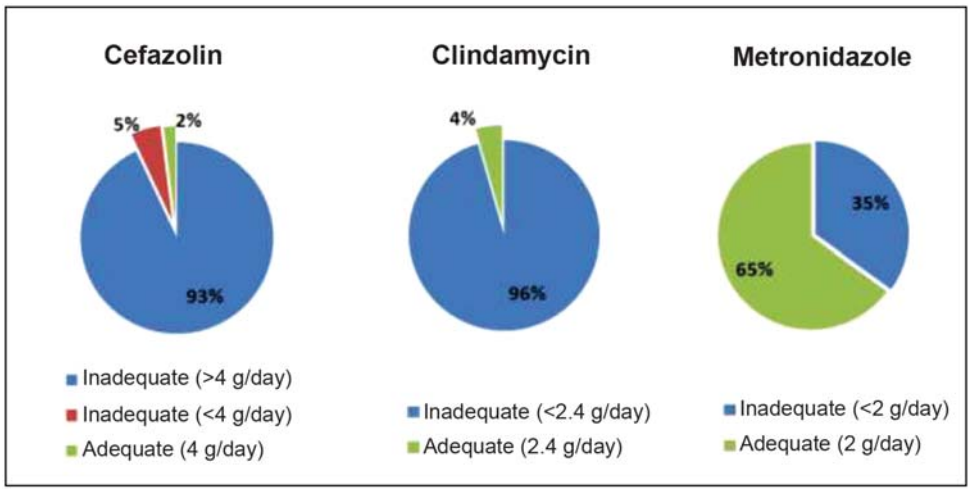

Fig. 2 Adequacy and inadequacy analysis of prescribed antimicrobial doses according to the Clinical Protocol "Primary Treatment of Exposed Fractures" - FHEMIG guidelines from June to December 2016, Hospital João XXIII, Belo Horizonte, Minas Gerais, Brazil.

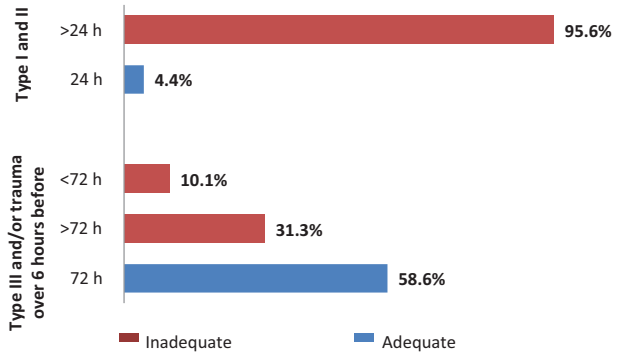

Fig. 3 Adequacy and inadequacy analysis of prescribed antimicrobial treatment duration according to the Clinical Protocol "Primary Treatment of Exposed Fractures" - FHEMIG guidelines from June to December 2016, Hospital João XXIII, Belo Horizonte, Minas Gerais, Brazil.

were obtained in patients with OF type I and II (95.6%), who were exposed to antimicrobial treatment for > 24 hours (►**Figure 3**).

The average duration of antimicrobial treatment in patients with type I and II OF was 4 days, ranging from 1 to 10 days; the CP, however, recommends treatment for only 1 day. In patients with type III OF and/or trauma occurring > 6 hours before, the average treatment duration was 3 days, ranging from 1 to 9 days, while the CP recommends it for 3 days. Overall, the average duration of antimicrobial treatment was longer in patients transferred to other units from the hospital network (4 days, ranging from 1 to 10 days) than in patients who remained at the primary care hospital (3 days, ranging from 1 to 8 days).

Regarding tetanus prophylaxis, the vaccination history from 207 (85.9%) OF patients were not found in the medical records, and no immunization was prescribed for them. Only

Table 4 Length of stay of patients with open fracture per fracture type and infectious complication, at the initial care hospital and after transfer to another unit from the hospital network.

Variables	Length of stay (Days)								
	Primary care hospital			Other unit from the hospital network			Total time at the hospital network		
	Mean	Median	Range	Mean	Median	Range	Mean	Median	Range
Fracture classification									
Type I	10	04	1–35	11	08	1–41	15	09	1–137
Type II	05	02	1–42	09	05	1–48	10	06	1–60
Type III	17	09	1–93	14	13	1–72	25	19	1–107
Unclassified	07	04	1–79	09	07	1–50	13	08	1–77
Infectious complication									
Without infection	07	04	1–079	07	04	1–41	12	07	1–77
With infection o	21	15	1–135	16	12	1–72	37	30	4–137
Total	0 9	04	1–135	11	8	1–72	16	09	1–137

34 (14.1%) patients were immunized, of which 28 (82.3%) were at the Intensive Care Unit (ICU).

As for the care flow, 124 (51.4%) OF patients were transferred to other units from the hospital network, 91 (37.8%) completed treatment at the primary care hospital, 21 (8.7%) were transferred to private hospitals, and 5 (2.1%) died. The average length of stay at the hospital network was 16 days, being longer in patients with type III OF (25 days) and in those with infectious complications (37 days), as shown in ►**Table 4**.

Discussion

With technological development and the increased diversity of existing diagnostic and therapeutic options, CPs have emerged to reduce the variability of adopted behaviors and to assist health professionals in the decision-making process to assure the quality and safety of patient care. The CPs are elaborated based on a comprehensive study of the best scientific evidence and consensus available in the literature on a given subject.[14]

The CP guiding this CA standardized antimicrobial treatment in the first care of OF patients according to fracture classification, which helps to choose the best treatment and predict the prognosis. Nevertheless, the study showed a significant frequency of fractures with no reported classification in the medical record. This inadequacy made it impossible to evaluate antimicrobials use in these fractures, except for those with trauma occurring $>$ 6 hours before, because its recommended regimen is the same as for type III fractures.

The epidemiological profile of the participants of the study was similar to that found in the literature, with young males mostly affected.[15–18] This finding can be explained by the greater exposure of young men to traffic accidents, especially with motorcycles.

The infection rate (18.7%) was consistent with the results from a study at an emergency hospital located in Canoas, state of Rio Grande do Sul, Brazil (18.8%).[18] However, other studies, one Brazilian[16] and one international,[19] found lower rates, of 10.0% and 13.2%, respectively. The significant association between infectious complications and type III fracture revealed by this CA is a well-established relationship in the literature.[18,19]

The CA also showed that the average waiting time for emergency surgery was 4 hours and 12 minutes, which is below the 6-hour limit recommended by the CP. In a Canadian study, the average waiting time was 9 hours and 15 minutes.[17] As in other publications, the present CA did not show any association between the waiting time for emergency surgery and the presence of infectious complications.[16,17]

The positive association between lower frequency of infectious complications and time from admission to antimicrobial treatment initiation was also observed in the descriptive study performed by Lack et al.[20] Although the CP recommends the preoperative institution of antimicrobial therapy without establishing a time limit between admission and treatment initiation, studies have shown that a delay in antimicrobial administration beyond 3 hours is related to a higher risk of infections.[21]

The fact that the highest rates of inadequate antimicrobial use occurred in type II and III OFs is worrisome, since these fractures are the most prone to infectious complications.[22]

The CP defined antimicrobial agent dosages based on OF epidemiological profile in the study scenario, that is, individuals with an average weight of 70 kg, and considering the predominance of otherwise healthy young adults. This standardization intends to facilitate antimicrobials management in emergency situations, as well as to ensure their rational use, avoiding inappropriate doses, frequencies and/or treatment durations. However, the CP does not predict situations with other patient profiles with OF, such as obese subjects, whose antimicrobial dose should be individualized and calculated according to body weight. As such, antimicrobial doses not standardized by the CP were considered inadequate even when they were within the therapeutic range established in the literature according to the body weight of the patient. Thus, it is important that these cases are predicted in the CP, increasing the flexibility of antimicrobial doses according to individual characteristics of the patients.[23,24]

The prolonged prescribed antimicrobial treatment duration was a surprising result, especially in type I and II OFs, when the average treatment time was four times longer compared to the CP recommendation. It is also worth mentioning that the longest antimicrobial treatment duration occurred in the transition from primary care to other units from the hospital network, probably due to a failure in consulting medical records about the time of antimicrobial use at the first hospital. Despite controversies among several authors about the appropriate duration of antimicrobial treatment, current studies show that increased exposure does not reduce infectious complications rates.[25,26] A retrospective case-control study comparing infection rates in OF patients undergoing antimicrobial treatment for periods ranging from 1 to $>$ 5 days did not indicate significant differences in the risk of infection, including in type III OF.[25] In addition to not being beneficial, prolonged antimicrobial treatment is related to an increased risk of adverse events, development of bacterial resistance, increased length of hospital stay and increased care-related costs.[5,6]

Regarding tetanus prophylaxis, the CP only mentions that it must be performed, without detailing the procedures, which should be based on national guidelines.[11] The CP only recommends the association of metronidazole for patients with unknown or uncertain vaccination history due to its antianaerobic activity, which reduces bacterial loads at the inoculation focus and prevents the production of tetanus toxin.[27] However, metronidazole administration does not exclude the need for immunoprophylaxis. During the audited period, there was no vaccination history records for all OF patients, which was considered a serious inadequacy given the probable missed opportunities for immunization. Thus, in all OF cases, it is necessary to verify and register the vaccination of the patient in the medical record, allowing adoption of the appropriate strategies.

The role of the clinical pharmacist in the ICU to review the basic care applicable to critically ill patients, including the investigation of vaccine status, may explain why most immunized OF patients were those admitted to this unit. Other studies reported the positive results of the participation of the pharmacist in trauma teams, reinforcing the significance of this professional as a member of the multidisciplinary healthcare team.[28]

A major limitation of the present study was the fact that the research evaluated only CP compliance by the traumatology team during the initial care of OF patients, not considering other comorbidities or injuries. This fact may have influenced our results, as subjects in more severe conditions could have their first orthopedic approach postponed to focus on most urgent issues, influencing the criteria evaluated in the study, such as waiting time for the first surgical approach, length of stay and incidence of infectious complications.

Conclusion

The present study identified divergences from the institutional clinical protocol; the most significant inadequacies were observed in the choice of antimicrobial regimens, doses and treatment duration, as well as in tetanus prophylaxis.

Conflict of Interests
The authors have no conflict of interests to declare.

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