Original Article
Efficacy assessment of two antibiotic prophylaxis regimens in oral and maxillofacial trauma surgery: preliminary results

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Abstract: The study set out to evaluate the efficacy of two antibiotic prophylaxis regimens in patients with facial fractures admitted to the Oral and Maxillofacial Surgery and Traumatology services of the Onofre Lopes University Hospital attached to the Federal University of Rio Grande do Norte in the period from December 2011 to December 2012. The sample consisted of 74 patients divided into two groups, GI with forty-three patients and GII with 32. Both groups received 2 g of cefazolin, 20 minutes before surgery. The postoperative protocol for each group was randomly determined; group I (single dose) received no antibiotics after surgery but group II (24 h dosage) received 1 g of cefazolin every 6 hours for 24 hours. Postoperative infection incidence was 9.3% (seven patients), six patients in Group I and one in Group II. 85% of the infections were in mandibular fractures. Results were presented qualitatively and quantitatively and the Chi square test (taking the value for p to be < 0.05) showed no statistically significant differences in the efficacies of the two regimens in the comparisons made between the cases of fractures in the upper and middle thirds of the face with those in the lower third (mandibular fractures). Considering mandibular fractures alone, Group II proved to be more efficacious with a p value of 0.02. However, to confirm the tendency shown in the mandibular fracture treatments whereby prolonging antibiotic administration for 24 hours appeared to be beneficial, research needs to be done with much larger sample groups.

Keywords: Postoperative infection, antibiotic prophylaxis, cefazolin

Introduction

Infection results from the presence of pathogenic micro-organisms and the alteration of homeostatic equilibrium between the individual and the environment [1]. When this complication affects postoperative sites it leads to retarded healing and an increase in overall treatment costs. In that light antibiotic prophylaxis seeks to reduce the levels of postoperative infection and the first researchers to evaluate the efficacy of such conduct associated to various surgical specialties were [2, 3]. They showed that antibiotics need to be administered 04 hours prior to any bacterial penetration because after that period, the rates of infection are similar to those found in cases where no such administration is undertaken.

While the literature abounds in antibiotic treatments and protocols for established infections there has been little emphasis on antibiotic prophylaxis [4, 5]. In the field of facial fracture surgery [6], were the first authors to show that the rates of infection in facial and mandible fractures went down from 42% to 9% and from 43% to 11% respectively, when antibiotics were administered prior to the incision as well as in the postoperative period. However, as they failed to report the type of antibiotic employed or the therapeutic scheme adopted, no guidelines for antibiotic prophylaxis were forthcoming. Recommendations regarding the form (via) of application, the use of narrow-spectrum medicines, pre-operative administration and the use of short-term dosage have been obtained from other separate studies [7, 8]. The

Table 1. Comparative analysis between the groups considering fractures of the upper and middle third. Natal/2014

| | | | Protocol | | Total | p |
			Single Dose	24 hours		
Infection	No	n	29	14	43	
		% Infection	67.4%	32.6%	100.0%	0.378
		% Protocol	96.7%	100.0%	97.7%	
	Yes	n	1	0	1	
		% Infection	100.0%	0%	100.0%	
		% Protocol	3.3%	0%	2.3%	

duration of antibiotic prophylaxis for mandibular fractures has been studied and it has been found that short-duration regimens are just as effective as long-term ones [9, 10]. There are still only a limited number of studies reported in the literature evaluating infection rates associated to fractures des-aggregated according to the three thirds of the face.

Facial fractures can take various forms according to their anatomical location, the etiological factor and the extent to which soft tissues are involved. Those aspects influence the possibility of infection occurring at the site of fracture reduction and fixation surgery [11], hence the importance of studies to evaluate the influence of those factors in postoperative infection development and the need to determine medicinal regimens or protocols capable of minimizing the occurrence of such complications.

That being so, the present prospective clinical study set out to evaluate the efficacy of two antibiotic prophylactic regimens used in oral and maxillofacial trauma surgery.

Materials and methods

Sample

Research participants were patients that had undergone surgery under general anesthetic for the reduction and/or fixation of facial fractures in the Oral and Maxillofacial Surgery and Traumatology services of the Onofre Lopes University Hospital affiliated to the Federal University of Rio Grande do Norte in the period from December 2011 to December 2012. The research project was submitted to the Hospital's Human Research Ethics Committee and duly approved under registration number 612/11.

The participants criteria were: 1) no gender restriction; 2) at the age of 15-70; 3) surgical-anesthetic risk categories should be I or II or III; 4) the facial fractures should show no signs of infection prior to surgery; and 5) not be allergic to the antibiotics used in the research.

Patients with pan-facial fractures or requiring surgery longer than six hours were excluded from the sample.

Study design

This clinical study was prospective, randomized and controlled. Patients underwent surgery for facial fracture reduction and fixation under general anesthetic. Prior to surgery, patients were randomly divided into two groups. Group 1 patients each received 2 g of Cefazolin (Cefazolin Sodium-Ampoule-1 g-*Genéricos Brasil*), administered intravenously but none was administered in the postoperative period. Group II patients received the same dose prior to the operation but in the postoperative period they also received 4 additional 1 g doses of Cefazolin intravenously, completing a 24 period of antibiotic prophylaxis. In the case of operations that lasted for more than 4 hours, an additional 1 g dose was given.

The surgical operations involved intra and extra-oral interventions and when required internal rigid fixation was undertaken using titanium plates and screws. Patients were given advice on oral hygiene procedures to be followed in the postoperative period that included chlorhexidine (0.12%) oral rinses and care to be taken with the surgical wounds.

Postoperative follow up was conducted in the 1st, 2nd, 4th and 6th weeks. The criteria used to determine the presence of infection were: a) pus drainage at the fracture site or in the vicinity of the surgical intervention site; b) increased swelling 7 days after the operation; c) presence of a fistula in the area of the surgical intervention or at the site of the fracture, with active drainage; d) other clinical features observed by the evaluator including typical signs of infection such as fever, edema, and localized redness.

Descriptive analysis was made of the independent variables, namely, age, sex, presence of

Table 2. Comparative analysis between the groups considering fractures of the lower third. Natal/2014

			Protocol		Total	p
			Single Dose	24 hours		
Infection	No	n	8	17	25	
		% Infection	32.0%	68.0%	100.0%	
		% Protocol	61.5%	94.4%	80.6%	0.020
	Yes	n	5	1	6	
		% Infection	83.3%	16.7%	100.0%	
		% Protocol	38.5%	5.6%	19.4%	

systemic diseases, trauma cause, drug use (tobacco, alcohol, marijuana, crack, cocaine, etc.), the time lapse between the trauma event and the surgical operation, length of the operation, and the measures adopted when infections were detected.

Statistical data was obtained using SPSS 17 software (SPSS Inc.®). The Chi-square bi-variable analysis test was used to check for statistically significant differences in infection evolution among the groups being assessed, adopting a probability value of P < 0.05.

Results

The research sample consisted of 74 patients, 42 of whom were included in Group I and 32 in Group II. 62 patients were males and 12 females. The prevailing age group among the patients was 30 to 40 and the commonest cause of trauma in the case of the facial fractures of this study was motorcycle accidents. Other causes included physical aggression, sports accidents and falls.

The commonest fracture sites found were the zygomatic-orbital complex (36%), followed by mandibular fractures (34%), nasal fractures (18%) maxillary fractures (7%) and frontal fractures (5%). 45 mandibular fracture sites were diagnosed and treated altogether and the mandibular region most affected was found to be the mandibular corpus (62%), followed by the symphysis and the angle (11% each), the chondyle and parasymphysis (7% each) and the ascending ramus (2%).

Group I comprised 42 patients (57.3%) and Group II 32 patients (42.7%). Of the total sample group, sever patients (9.3%) presented postoperative infection; 6 of them from Group I and 1 from Group II. Mandibular fractures

accounted for 19% of all infections that occurred in the sample. 38.5% of the fractures in Group I were mandibular, as were 5.6% of those in Group II.

The Chi-squared test revealed that there were no significant differences in antibiotic prophylaxis efficacy between groups I and II as regards the irruption of infection (p = 0,090). The same was true in regard to fractures in the upper third of the face and those in the middle third (Table 1). Differences were detected however in the case of fractures located in the lower third of the face (mandible). In the case of mandibular fracture treatments, the antibiotic prophylactic regimen adopted for Group I (single dose) was less efficacious than that adopted for Group II (24 h) with a p value of 0.020 (Table 2).

Surgical procedures lasted from 1 to 6 hours but most of them (28%) took from 2 to 3 hours. The interval between the trauma event and the surgical intervention varied from 1 to 8 weeks but in 68% of cases, surgery took place within 21 days. Statistical testing found no difference between the efficacy of the two antibiotic prophylaxis regimens related to the duration of the surgical operations or the interval between the trauma event and surgery (Tables 3 and 4).

Surgical access to the fractures was varied. 81% of the procedures involved cutaneous or mucosal access routes of which 49% were intraoral and 51% extraoral. In the case of patients that developed infections, no differences were detected associated to the type of access being intra or extraoral in either of the prophylactic regimens used (Table 5). In the case of patients with teeth present in the fracture line that hampered fracture reduction or that showed signs of caries or periodontal infection, the teeth were extracted.

In Group I, there was 1 patient with a zygomatic-orbital complex fracture and 5 with mandibular fractures. In the latter case the angle was the mandibular region most affected (n = 3). In the case of one of these 3 patients, the third molar was removed, in another it was maintained and in the third there was no tooth present in the fracture line. Only one patient in Group II developed an infection in the mandibu-

Table 3. Relationship between time of surgery and infection of groups I and II, in infected patients. Natal 2014

			Group I	Group II	Total	P
Time of surgery	0-3 h	n	3	1	4	
		% Time of surgery	75.0%	25.0%	100.0%	
	3-6 h	n	3	0	3	0.265
		% Time of surgery	100.0%	0%	100.0%	

Table 4. Time elapsed trauma until surgey between group I and II, in infected patients. Natal 2014

			Group I	Group II	Total	P
Time to surgery	1 week	n	1	0		
		% Time to surgery	100.0%	0%	100.0%	
	2 weeks	n	2	0	2	0.248
		% Time to surgery	100.0%	0%	100.0%	
	4 weeks	n	1	0	1	
		% Time to surgery	100.0%	0%	100.0%	
	5 weeks	n	0	1	1	
		% Time to surgery	0%	100.0%	100.0%	
	6 weeks	n	2	0	2	
		% Time to surgery	100.0%	0%	100.0%	

lar angle region. None of the patients that developed infections showed any signs of systemic immunosuppressive diseases and only one of them regularly used tobacco.

Oral administration of antibiotics was used to treat the infections, generally in doses of 500 mg of Amoxicillin every 8 hours for 10 days during which time the site of the surgical intervention was irrigated with 0.12% chlorhexidine digluconate. Abscesses were surgically drained and treatment with metronidazole introduced. None of the patients required surgery under general anesthetic for fixation device removal and in all of them fractures were consolidated and the final result unimpaired.

Discussion

Antibiotic drug selection is based on criteria that include, its spectrum of action, availability in the health service and the quality of being a pharmaceutical with few reported adverse reactions

Cefazolin, according to [5, 12, 13], has been widely used in antibiotic prophylaxis associated to surgical procedures in a variety of services in view of its low cost and its action against *Staphylococcus aureus,* always present in the

micro biota of the skin and mouth and currently considered to be the major cause of the postoperative infection of surgical wounds. In the light of those advantages, the study aimed to assess cefazolin as a prophylactic antibiotic. The alternative available for patients allergic to penicillin is clindamycin, which, however, has the disadvantage of broad spectrum action and the possible development of pseudomembranous colitis as reported by Hurley & Nguyen [14].

The advantages of antibiotic prophylaxis have been investigated since as far back as 1963 when Strong reported no detectable benefits stemming from such treatment in ear nose and throat surgery. The authors [16, 17] in 1976, were the first to discuss the ideal conditions for conducting antibiotic prophylaxis. Authors like [6, 18] studied the application of antibiotic prophylaxis associated to facial trauma surgery and they reported positive results for the procedure insofar as postoperative infection rates were reduced to less than 10% of their former levels. The overall infection rate observed in the present study was 9.3%, very much in keeping with the results reported in the respective literature.

The controversy surrounding the ideal duration for such treatment has been addressed by various studies. In 1983, Aderhold made an assessment of 120 fractures that had been treated using rigid internal fixation technique. The patients were divided into 03 groups. The first group was only given antibiotics right after surgery; for the second, antibiotics were continued after surgery for 48 hours and for the third the period was extended beyond 48 hours. The type of antibiotic used and the form of administrating it were not reported. Their study findings revealed that the infection rate for group 1 was 20% and there were no differences found in the comparisons with the other two groups (*P* <

Table 5. Intra and extraoral surgical accesses versus infection in Groups I and II

			Protocol		Total	p
			Single Dose	24 hours		
Incision	Intra-Oral	n	4	1	5	
		% Incision	80.0%	20.0%	100.0%	
	Extra-Oral	n	2	0	2	0.390
		% Incision	100.0%	0%	100.0%	

sity of antibiotic prophylaxis in treating fractures of the middle third of the face. Our study, however, did not specifically address that aspect.

Mandibular fractures are at greatest risk of developing infections, especially in the tooth-bearing sections, because the gingival sulcus favors fracture contamination via exposure to the oral environment and that makes it imperative to prescribe antibiotic prophylaxis. In keeping with the findings of [19, 20] studies, the mandibular fracture infection rates registered by our study were statistically significant in comparison with those for fractures in the middle third of the face. There was also statistically significant difference between the two groups in the comparisons of mandibular fraction infection rates (chart 2). In group I (single dose) the infection rate was high 38.5%, comparable to that for cases in a review published Peterson [23] reporting on a series of studies in which infection rates ranging from 22 to 50% were associated to surgical treatments for mandibular fractures in which no antibiotic prophylaxis was undertaken. The infection rate for Group II was 5.6% showing the regimen's superior efficacy in preventing infection with results approaching those obtained by [24, 9] their respective studies. Thus, our study findings clearly demonstrate that keeping up antibiotic administration for at least 24 hours into the postoperative period seems to reduce infection rates in mandibular fracture treatment.

The literature shows that factors associated to the patient himself can also have an influence on infection development. The abusive consumption of substances such as illicit drugs, alcohol and tobacco could alter fracture healing processes and increase the rate of complications [25]. Other authors were able to show that higher infection rates were also associated to the presence of systemic diseases in patients [26]. We feel there is a need to identify such aspects of the patient's profile in order to compensate for their influence and in such cases prolonged antibiotic therapy should be the rule. In our study, the sample numbers were too small to confirm the last mentioned relations as tobacco use was only registered by one of the patients that became infected.

0.05). It was therefore concluded that there is no need to prolong the administration of antibiotics in the postoperative period to diminish infection rates. Other authors like [20, 21] reported evidence that antibiotic prophylaxis conducted for short periods is just as effective as prophylaxis for long periods and they also showed that it was necessary to repeat doses of the antibiotic during surgical operations that last more than four hours.

The limitations of those studies are the differences among the procedures adopted, the lack of specified criteria for determining the presence of infection and the variations in duration among the therapies used. Nevertheless, they do show the benefits of using short-duration antibiotic prophylaxis insofar as it avoids the development of adverse side effects, allergies and super-infections stemming from the development of resistant strains. Well-delineated studies investigating antibiotic prophylaxis in mandibular fracture treatment were conducted by [9, 10], and they demonstrated that there was no difference between the infection rates when single dose regimens were used and those when the doses were continued on into the postoperative period. Based on those findings, this study opted to only assess short-duration regimens of antibiotic prophylaxis, in keeping with the worldwide tendency.

In our study, fractures located in the middle third of the face including those of the zygomatic-orbital complex showed infection rates compatible with those reported in the literature. In their study of 134 treated zygomatic-orbicular complex fractures, were found only 2 cases of infection and our study, just 1 (3%) of the 33 patients with fractures in the middle third of the face developed an infection [22]. The case in question was a zygomatic-orbital complex fracture treated by both intra and extra-oral access. There is thus a need to evaluate the real neces-

The time lapse between the trauma event and the onset of definitive treatment was one of the factors that [27] analyzed in their studies and they considered delayed access to treatment to be a determinant factor in infection development. Furthermore they observed that such delays were associated to an uncooperative attitude towards treatment on the part of the patient. No relation was found in the present study between delayed treatment onset and higher infection rates confirming, in this case, the findings of [6, 28].

Our findings also failed to detect any relation between longer operating period and infection development in either of the groups studied. Considered that shorter operating time (under 3 hours) and the nonuse of intermaxillary fixation contributed to ensuring greater comfort in the postoperative period and a shorter hospital stay for the patient. It must be stressed that, in our sample, most of the operations involved were within that time span and that the use of internal rigid fixation and the exclusion of patients with intermaxillary fixation may well have contributed to the low levels of infection observed [29].

Preliminary results show the efficacy of the two regimes that were employed in the cases of facial fracture surgery. What is needed, however, is to increase the sample size to enhance the statistical significance and confirm the tendencies suggested by the preliminary results whereby greater efficacy in preventing infection as associated to trauma surgery for fractures in the lower third of the face was observed for the Group II treatment (24 hours).

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Disclosure of conflict of interest

None.

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