Journal of Health, Medicine and Nursing
ISSN 2422-8419 An International Peer-reviewed Journal
Vol.97, 2022

Comparison between Ceftriaxone with Ceftriaxone and Metronidazole Combination in Maxillofacial Fracture (at KSM Reconstruction and Aesthetic Plastic Surgery, RSUD Dr. Soetomo)

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Abstract
The purpose of the research is to evaluate infection rate on maxillofacial fracture in Plastic Surgery and Aesthetic at Dr.Soetomo General Hospital Surabaya, Indonesia, from January 2015 to December 2019. The research is an analytic descriptive study with retrospective cohort design. The affordable population were maxillofacial fracture patients with reconstructive treatment who were given therapeutic antibiotics, namely ceftriaxone at a dose of 2 x 1 g and metronidazole 3 x 500 mg intravenously. The collected data is then transferred to IBM Statistical Package for Social Sciences (SPSS) 20 software for statistical analysis with non-parametric statistics. Descriptive and analytical data will be presented in a series of texts and tables. A total of 621 patients medical record were obtained with a characteristic distribution based on gender, age, and history of trauma from 2015 to 2019 where total cases of postoperative infection after facial bone fracture reconstruction were 10 patients (1.61%), the incidence of infection with a single antibiotic ceftriaxone were 6 patients (0.97%) and cases in the administration of combination of antibiotics ceftriaxone, metronidazole were 4 patients (0.64%). The incidence of post-operative infection for facial fracture reconstruction given single ceftriaxone antibiotics was higher than that given the combination of ceftriaxone, metronidazole at KSM Reconstructive and Aesthetic Plastic Surgery, Dr. Soetomo General Hospital, Surabaya, Indonesia from 2015 until 2019.
Keywords: *ceftriaxone-metronidazole,* infection, maxillofacial fracture
DOI: 10.7176/JHMN/97-03
Publication date: January 31st 2022

1. Introduction

1.1. Background

Maxillofacial trauma is the term used when discussing injuries to the facial skull. Sometimes the term craniomaxillofacial is more appropriate because in this type of injury, the anterior wall and floor of the anterior cranial fossa are also affected (Kellman, 2021). Maxillofacial injuries are one of the most common causes of visitation to the emergency department, ranging from fractures to extensive facial damage that require complex treatment (Jose et al., 2016). Accurate reconstruction of the skull is necessary in order to maintain facial aesthetics and also soft tissue care and has an important impact on critical functions such as vision and chewing (Kellman, 2021). The surgical wound itself has a risk of contamination which is divided into several types, namely clean wounds, clean contaminated wounds, contaminated wounds, dirty or infected wounds according to the Centers for Disease Control and Prevention (Azari and Bell, 2016). Open fractures and soft tissue wounds that show no signs of infection are considered contaminated at the time of repair. Traumatic wounds can become infected due to the presence of bacteria or debris from the environment during repair (Hom, 2009). An algorithm for wound debridement, irrigation, and antibiotic prophylaxis should be used as a reference when performing surgical interventions (Azari and Bell, 2016).

1.2. Literature Review

Traumatic facial fractures are predominantly caused by accidents worldwide. The incidence of mandibular and maxillary fractures was the highest among other bones, which was 29.85%, followed by zygomatic fractures 27.64% and nasal fractures 12.66% (Ghazali, 2007). Data on Reconstructive and Aesthetic Plastic Surgery at Medical Staff Group, Dr. Soetomo General Hospital Surabaya, showed that cases of facial fracture trauma received at the emergency unit were 69 cases in 2018 and 74 cases in 2019

Postoperative wound infection is a health problem that often occurs and involves a complex process. Cases of postoperative infection must be treated properly because wound infection is responsible for a fairly high level of morbidity and mortality (Zabagio and Sharman, 2020). Infection can manifest locally, but if the infection has become progressive, systemic signs such as weakness or fever will appear (Pisculli, Barker and Farrell, 2011). Maxillofacial trauma post-op infection is a problem that has the potential to create serious problems for patients.

Giving antibiotics in post-traumatic facial reconstruction surgery is expected to prevent cases of infection. Dr. Soetomo General Hospital is a type A hospital which is a referral center hospital for East Java Province. Dr. Soetomo General Hospital has various cases of facial fracture reconstruction ranging from simple to complex

cases. The antibiotic regimen given in the case of post-traumatic facial fracture reconstruction at KSM (Medical Staff Group) Reconstructive and Aesthetic Plastic Surgery, Dr. Soetomo General Hospital, Surabaya, was divided into two, namely the administration of ceftriaxone antibiotics alone or the administration of ceftriaxone and metronidazole, if the type of case of maxillofacial trauma involved intraoral structures. According to a study by Saikat, the combination of a third-generation cephalosporin with metronidazole provided a better antibacterial outcome in maxillofacial trauma infections. These findings combined therapy with ceftriaxone and metronidazole with different mechanisms had a lower effect on the number of postoperative wound infections compared with the use of cefazolin antibiotics or single cephalosporin antibiotics (Saikat, 2016).

The facial area contains skin and mucosa that are rich in bacteria, but do not have large muscle mass. Facial trauma can be widespread and can be life-threatening if it involves the airway. Oral mucosal structures prevent bacterial contamination of deeper facial structures, but deeper trauma increases the risk of infection. Anaerobic bacterial infections and actinomycetes can occur when trauma to the mouth occurs (Bayston et al, 2000). In a study conducted by Heit *et al*. in 1997 with a total of 90 mandibular fracture patients who were given ceftriaxone prophylaxis 1 g per day compared to 2 billion units of penicillin, two patients had infections in each group (Andreasen, 2006). Metronidazole is an antibiotic for anaerobic bacteria used with a combination of chloramphenicol antibiotics, ampicillin in brainstem trauma patients (Petersen and Waterman, 2011). Till now, there is no studies about infection rates in post-op patients with maxillofacial trauma which was only received ceftriaxone compared to patients receiving a combination of ceftriaxone and metronidazole at Dr. Soetomo, General Hospital, Surabaya.

1.3. Research Method

This study is a retrospective study, using recorded clinical data at Dr. Soetomo General Hospital from 2015 to 2019 through recording patient's data on infection cases after reconstruction of facial fractures.

1.4. Research Purpose

This research aims to find out cases of postoperative infection by giving different antibiotic therapy at KSM Reconstructive and Aesthetic Plastic Surgery Dr. Soetomo General Hospital, so that in the future, the basic data obtained can be applied and become a protocol in the administration of antibiotics to maxillofacial patients.

2. Material and Methods of Research

This study is a descriptive analytic study with a retrospective cohort design to examine the outcome of wound infection in facial fracture reconstruction surgery. The target population is maxillofacial fracture patients with reconstructive treatment given therapeutic antibiotics. The affordable population were maxillofacial fracture patients with reconstructive treatment who were given therapeutic antibiotics at Dr. Soetomo General Hospital, Surabaya. The research subjects were the affordable population that met the inclusion criteria.

2.1. Research Time

This research was conducted in June 2021 by collecting medical records of patients who met the inclusion and exclusion criteria who ever treated at Dr. Soetomo General Hospital, Surabaya, and Department/KSM of Reconstructive and Aesthetic Plastic Surgery, Faculty of Medicine Airlangga University/ Dr. Soetomo General Hospital, Surabaya from 2015 to 2019.

2.2. Research Material

The subject of this research is medical record data of surgical wound infection at KSM Reconstructive and Aesthetic Plastic Surgery Dr. Soetomo General Hospital during the period of January 2015 to December 2019.

2.3. Inclusion Criteria

1) Physical Maxillofacial examination data at SMF Reconstructive and Aesthetic Plastic Surgery Dr. Soetomo General Hospital, Surabaya from 2015 to 2019 which experienced post-operative infection
2) Reconstructive surgery patients with facial trauma who were given antibiotics ceftriaxone or ceftriaxone and metronidazole at a dose of 2x1 g ceftriaxone, and 3x500 mg metronidazole intravenously for 5 days.

2.4. Method of Sampling.

This study uses secondary data derived from the medical records of Dr. Soetomo General Hospital Surabaya. The information that will be taken is in the form of the patient's gender, age, diagnosis, type of antibiotic used, and the results of post-reconstruction control.

Samples were taken by tracing the medical record data of patients diagnosed with facial bone fractures who suffered a maxillofacial injury and received reconstruction management at Dr. Soetomo General Hospital, Surabaya, from 2015 until 2019. Patients who meet the inclusion criteria will be included in the sample study.

The data obtained from the medical record was then processed using Microsoft Excel 2013 software, so that it can be analyzed. Several steps in data processing include, editing to check if the data obtained is relevant; coding is done to simplify the software language analysis by converting it into numbers. After that, processing is carried out so that the data that has been entered can be analyzed, and finely is cleaned or cleaning of data entry errors.

2.5. Data analysis.

The collected data is then transferred to the IBM Statistical Package for Social Sciences (SPSS) 20 software, to be analyzed with non-parametric statistics. Descriptive and analytical data will be presented in a series of texts and tables.

The patient's data obtained during the study were guaranteed to be confidential by the researcher and has been approved by the ethics committee of Dr. Soetomo General Hospital, Surabaya, Indonesia (0739/108/4/ V/2021).

3. Results And Discussion

3.1. Subject Characteristics

There was a total of 621 patients data distributed characteristically based on gender, age, and history of trauma from 2015 to 2019.

3.1.1. Gender

Reconstructive surgery patients with facial trauma injuries by gender during 2015 to 2019 were shown in Table 1

Table 1. Distribution of patients by sex

Gender	2015		2016		2017		2018		2019		2015-2019	
	n	%	n	%	n	%	n	%	n	%	n	%
Man	115	79,86	60	88,23	96	81,35	92	74,20	127	75,60	490	78,9
Woman	29	20,14	8	11,77	22	18,65	31	25,20	41	24,40	131	21,1
Total	144	100	68	100	118	100	123	100	168	100	621	100

n : frequency % : percentage

Table 1 showed the number of reconstructive surgery patients with facial trauma who met the inclusion criteria from 2015 to 2019 were 490 males (78.9%), higher than that in female of about 131 (21.1%). In 2015 there were 115 males (79.86%) and 29 females (20.14%); in 2016 60 (88.23%) men and 8 (11.77%) women. In 2017 there were 96 (81.35%) men and 22 (18.65%) women. In 2018 there were 92 (74.20%) men and 31 (25.20%) women. In 2019 there were 127 (75.60%) men and 41(24.40%) women. These results showed that male sex in maxillofacial fractures is more dominant than female.

3.1.2. Age

In this study, ages were differentiated based on the WHO classification, namely infants 0-1 years, children 2-10 years, adolescents 11-19 years, adults 20-60 years and the elderly over 60 years. Age classification based on WHO, can also be used to determine health risk factors and develop preventive measures. Distribution of facial trauma injury reconstructive surgery patients by age was shown in Table 2

Table 2 Distribution of Patients by Age

Age	2015		2016		2017		2018		2019		2015-2019	
	n	%	n	%	n	%	n	%	n	%	n	%
Children	2	1,30	2	2,95	2	1,69	4	3,25	3	1,78	13	2,19
Teenager	32	22,32	17	25,00	26	22,05	18	14,63	22	13,10	115	19,42
Mature	110	76,38	49	72,05	86	72,88	99	80,48	139	82,76	483	76,91
Elderly	0	0,00	0	0,00	4	3,38	2	1,64	4	2,36	10	1,48
Total	144	100	68	100	118	100	123	100	168	100	621	100

n = frequency , % = percentage

Table 2 showed that the age of maxillofacial fracture patients from 2015 to 2019 were 76.91% or 483 adults, followed by 19.42% or 115 adolescents, 2.19% or 13 children and 1.48% or 10 elderlies. Based on this data, it is assumed that the highest incident of maxillofacial fracture in adult age was due to that the adult age is a productive age with high mobility especially using motorcycle. This is in line with Kraus *et.al*. (2003) who stated that this age group has the highest traffic accidents, so it is possible that this age is more susceptible to maxillofacial trauma.

Similar study based on age in maxillofacial fracture by Kesuma and Bangun (2009) in Eben E Manalu

(2018) conducted at RSCM Jakarta, found that the average age of maxillofacial trauma was 27.5 ± 11.5 years. The data collected at the Reconstructive and Aesthetic Plastic Surgery KSM Reconstructive and Aesthetic Plastic Surgery, Faculty of Medicine, Airlangga University, Surabaya showed that adults age was the most people, of 483 adults (76.91%) experienced maxillofacial fracture since this adult age has the highest mobility

3.1.3 Patient History

Patient data based on injury history from diagnosis of maxillofacial fracture based on fracture location in one facial area or all facial areas at Dr. Soetomo General Hospital, Surabaya and KSM Reconstructive and Aesthetic Plastic Surgery Airlangga University, Surabaya from 2015 to 2019 was shown in Table 3

Table 3 Distribution of patients by diagnosis of a single facial fracture

Diagnosis Facial Fracture	2015		2016		2017		2018		2019		2015-2019	
	n	%	n	%	n	%	n	%	n	%	n	%
Frontal/Orbital	3	2,08	5	7,35	1	0,84	1	0,81	4	2,38	12	1,93
Parietal	3	2,08	3	4,41	12	22,88	29	23,57	33	28,57	150	24,15
Nasal	0	0	0	0	0	0	5	4,06	6	3,57	21	3,38
Lacrimal	25	17,36	25	36,78	15	12,71	9	7,31	7	4,16	29	4,68
Zigomatic	29	31,25	1	1,47	13	12,71	21	17,07	28	16,66	114	18,36
Ethmoid	3	2,08	5	7,35	1	0,84	1	0,81	4	2,38	12	1,93
Maxilla	39	34,72	4	5,58	43	41,52	21	18,70	28	30,35	175	28,18
Mandibula	12	8,33	24	35,29	12	12,71	29	17,88	20	11,90	102	16,42
Unclear	1	1,38	0	0	3	4,22	1	0,81	1	1,18	6	0,97
											621	100

Table 4 Distribution of patients by classification of fracture diagnosis

Diagnosis of Facial Fracture	2015		2016		2017		2018		2019		2015-2019	
	n	%	n	%	n	%	n	%	n	%	n	%
Single	47	33,10	10	14,93	42	35,29	44	35,48	64	37,87	207	33,34
2 area	59	41,55	31	46,27	38	31,93	34	27,42	54	31,95	216	34,78
Panfacial	36	25,35	26	38,80	39	32,77	46	37,10	51	30,18	198	31,88
Total	142	100	67	100	119	100	124	100	169	100	621	100

n = frequency, % = percentage

Table 3 showed the injury history of patients who were not infected or infected after surgery and had administrated ceftriaxone antibiotics and the combination of ceftriaxone, metronidazole in Maxillofacial fractures. It was shown that the highest number of injury obtained from patients which met the inclusion criteria was in maxilla bone, of about 175 patients (28.18%), followed by parietal 150 patients (24.15%), zygomatic 114patients (18.36%), mandible 102 patients (16.42%), orbital, nasal, lacrimal, ethmoid and patients with a diagnosis of panfacial type facial fracture, were about 198 patients (31.88%).

The most common etiology of facial fractures are motorcycle accidents, violence, and work accidents (Tahereh *et al*., 2015). Several recent studies conducted at some hospitals trauma unit in several countries showed that the incidence of maxillary fractures was more associated with mandibular fractures. Other data reported from trauma center level, showed that among 663 patients with facial bone fractures, only 25.5% were maxillary fractures (Eben, 2018).

Maxillary fracture is a form of trauma to the face that often caused by mainly motor vehicle accidents. Treatment of maxillary fractures not only considers functional but also aesthetic issues. The fracture pattern that occurs does not always follow the theoretical Le Fort I, II, and III pattern, but is more often a combination of these classifications. There are some basic things about maxillary fractures i.e: 1. For maxillary fractures to occur, whether Le Fort I, II, or III, the pterygoid process must be disrupted; 2. The presence of mobility and malocclusion on physical examination is a hallmark of maxillary fracture although not all maxillary fractures cause mobility; 3. Radiological examination, either plain X-ray or CT scan is needed to confirm the diagnosis, but CT scan is the main choice; 4. Maxillary fractures generally have a fairly good prognosis if the treatment is carried out quickly and appropriately, but complications which may lead to disability or death could arise, if it is not handled properly; 5. Maxillary fractures in children are different from adults because of a more prominent growth and development in children. The maxillary structure has a sinus cavity, which produces secretions to moisten the cavity, trapping dust and bacteria, so that in the case of maxillofacial fractures, it is a good medium for bacteria to grow and increase the risk of infection.

3.2 The Relationship Between Ceftriaxone Antibiotics and Ceftriaxone, Metronidazole Combination with Postoperative Infections of Maxillofacial Fractures

The data obtained were tested by chi-square. The results showed, the relationship between the administration of ceftriaxone antibiotics and the combination of ceftriaxone, metronidazole and infection in maxillofacial fractures at KSM Reconstructive and Aesthetic Plastic Surgery Dr. Soetomo General Hospital, Surabaya in 2015 until 2019 was shown in Table 5

Table 5 The Relationship Between Administration of Ceftriaxone Antibiotics, Ceftriaxone, Metronidazole Combination and Infection after Surgery on Maxillofacial Fractures

Antibiotic	Infections of Maxillofacial Fractures						
	Not Infected		Infected		Chi Square Acount	Chi Square Table	Significance *(a)*
	n	%	n	%			
Ceftriaxone and *Metronidazole* Combination	611	98,39	4	0,64	0,0483	0.016	0,000
Ceftriaxone			6	0,97	11,477	3.825	0,000
Total	611	98,39	10	1,61	11,526	3,841	0,000

n = frequency , % = percentage

Table 5. showed that the relationship between administration of ceftriaxone antibiotics and the combination of ceftriaxone, metronidazole, to infection after surgery in maxillofacial fractures at KSM Reconstructive and Aesthetic Plastic Surgery Dr. Soetomo General Hospital, Surabaya in 2015 to 2019, was significant, since the resulted p-value is 0.000 ($p < 0.05$). The value of the Chi-Square test is 11.526; on the other hand the value of the chi-square table (T table) for df (degrees of freedom) = 1 at a significance of 0.05 is 3.841. Since the calculated chi square value > chi square table value, it can be concluded that null hypothesis is rejected and the result is accepted, thus the results of this study indicated that there was a significant relationship between the administration of the antibiotic ceftriaxone and the combination of ceftriaxone, metronidazole, to infection after surgery for maxillofacial fractures.

Table 5. also showed that from 621 medical records of patients who received antibiotics or 100%; 98.39% of those had no infection and 1.61% of those develop an infection. The results of this study was supported by Andayani and Riswaka (2005) who stated that 100% of patients at the PKU Muhammadiyah Hospital in Yogyakarta, received prophylactic antibiotics followed by the administration of therapeutic antibiotics. Furthermore Gondo (2007) stated that the combined use of antibiotics has several advantages such as reducing resistance to antibiotics because the use of synergistic combinations of antibiotics can increase the ability of antibiotics to kill germs. In addition, the use of antibiotics in combination can reduce the toxic effects of drugs because the lower the dose of each type of antibiotic given, the lower the toxicity. In a study at Bethesda Hospital with 30 cases of acute appendicitis surgery, given a combination of ceftriaxone and metronidazole antibiotics, the infection rate was low (Sander, 2015). The use of single therapy antibiotics in this case was caused by the patient's ability to receive antibiotics orally. Most patients who receive antibiotics intravenously can safely be switched to oral therapy 24 hours later if their clinical condition improves, such as an improvement in signs and symptoms of infection (Anonymous, 2009).

The results of statistical analysis with the hypothesis that the risk of infection after facial fracture reconstruction surgery is lower in the administration of a combination of antibiotics ceftriaxone and metronidazole compared to the administration of a single antibiotic ceftriaxone at the Reconstructive and Aesthetic Plastic Surgery KSM Dr. Soetomo General Hospital, Surabaya in 2015, 2016, 2018, 2019; the null hypothesis test was accepted ($p < 0.05$), while in 2017 the null hypothesis test was rejected ($p > 0.05$). These indicate that the research hypothesis is statistically significant.

3.3 Estimation of the Curve of the Relationship Between Ceftriaxone Antibiotics and the Combination of Ceftriaxone, Metronidazole and Postoperative Infection of Maxillofacial Fractures

Estimation of the curve of the relationship between the independent variables, namely the administration of ceftriaxone antibiotics and the combination of ceftriaxone, metronidazole with the dependent variable, namely infection after surgery for maxillofacial fractures: linear, exponential or quadratic as shown in Table 6.

Table 6 Estimation of the Curve of the Relationship Between Ceftriaxone Antibiotics and the Combination of Ceftriaxone, Metronidazole and Postoperative Infection of Maxillofacial Fractures

Equation	Model Summary					Estimation Parameter		
	R Square	F	df1	df2	Sig.	Constant	b1	b2
Linear	.019	11.706	1	619	.001	1.931	.034	
Square	.	.	.	.	.	1.984	.000	.000
Exponential	.019	11.706	1	619	.001	1.907	.024	

Table 6. showed that the p value on Estimation of linear and exponential curves was lower than 0.05 ($p <$

0.05). Thus, the estimation of the curve of the relationship between the independent variables, namely the administration of the antibiotic ceftriaxone and the combination of ceftriaxone, metronidazole with the dependent variable, is linear and exponential to postoperative infection of maxillofacial fractures and from the results of the model's description analysis was exponential (Curve model like Figure 1)

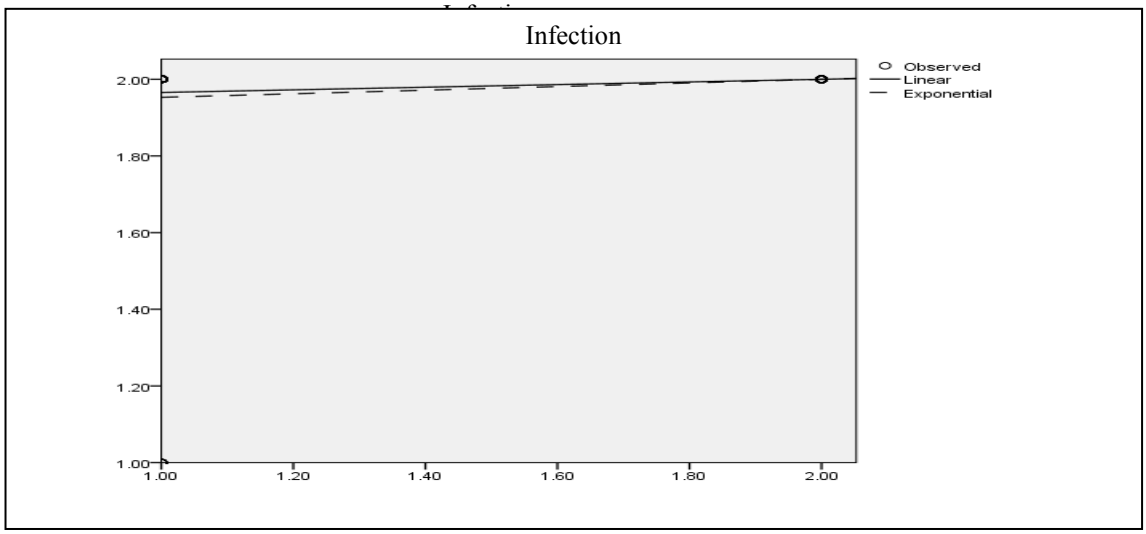

Figure 1. The Curve Model of the Relationship Between the Administration of Ceftriaxone Antibiotics And the Combination of Ceftriaxone, Metronidazole and Infection after Surgery in Maxillofacial Fractures

4. Conclusion

The incidence of post-operative infection of facial fractures was higher in the administration of single ceftriaxone antibiotics compared to the combination of ceftriaxone, metronidazole at KSM Reconstructive and Aesthetic Plastic Surgery, Dr. Soetomo General Hospital, Surabaya from 2015 until 2019.

5. Suggestion

It is recommended to use combination of antibiotic ceftriaxone and metronidazole therapy in cases of maxillofacial fracture surgery compared to single antibiotics.

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