Systemic Corticosteroid Therapy for Steven Johnson Syndrome (SJS): Toxic Epidermal Necrolysis (TEN) Inhospitalized Patients of Dr. Moewardigeneral Hospital Surakarta January 2016-December 2017

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Abstract: This retrospective descriptive study was conducted in hospitalized patients ofDr. Moewardi General HospitalSurakarta between January 2016 and December 2017. The secondary data were taken from medical record.The total number of patients was 26 people with the most age affected was 46 - 55 years and 56 - 65 years (23%). Male (57%) tended to be more affected than female (42%). The most common diagnosis was SJS(61%) followed by SJS overlap TEN (19%) andTEN (19%).Hypertension was the most comorbid disease (15%), mucosal involvement mostly affected mouth (88%) and the causes of SJS – TEN mostlyinvolved more than one drug (53%). Most suspected causative drugs were cephalosporin and paracetamol (23%). The average duration of systemic corticosteroid therapy was 10 days with an average dose 25 mg per day (1.5 mg / kg body weight / day). Treatment of systemic corticosteroids in cases of SSJ - NET in Dr. Moewardi General Hospital Surakarta showed clinical improvement with an average of 10 days treatment and an average dose of 25 mg per day, tappering dose.

1 INTRODUCTION

Epidermal Necrolysis (EN) is an acute mucocutaneous syndrome with symptoms of necrosis and scalling inepidermal leading to mortality.[1] Epidermal Necrolysis is classified into several types of severity based on the area of the body involved,below 10% is SJS, 10% - 29% is SJS overlap TEN and 30% is TEN.[2] The incidence rates of SJS and TEN are 1,2 – 6 and 0,4–1,2 per million people annually, respectively (Valeyrie-Allanore, 2012; Gupta et al., 2016).

Most cases of SJS – TEN are induced by drugs (Kariosentono, 2015). Although all drugs can be the etiology but most of the reactions are associated with several high-risk drugs such as carbamazepine, phenytoin,allopurinol, lamotrigine, oxycam, Non Steroid Anti Inflamasi, sulphonamides, cephalosporin and nevirapin (Maciejewska et al., 2014; Gupta et al., 2016).

The success rate of SJS – TENtreatment depends on the stage at which treatment begins, the age of the patient, the degree of necrolysis, comorbidity, complications (electrolyte imbalance, renal or hepatic dysfunction, Adult Respiratory Distress Syndrome - ARDS and sepsis), availability of drugs and clinicians (Gupta et al., 2016). One of the treatments for SJS – TENissystemic corticosteroids because both of these diseases aremediated by the immune system and corticosteroids have the effect of suppressing the intensity of the reaction, preventing or decreasing skin necrolysis, reducing fever and discomfort as well as breaking down internal organs when given in the early stages and high doses (Gupta et al., 2016).

Due to the lack of data on SJS – TEN and the use of systemic corticosteroid in Indonesia in general and Dr. Moewardi General Hospital in particular, therefore we conducted this study to provide an overview of SJS – TEN patients as well as systemic corticosteroid therapy, in order to improve the therapeutic quality and management of SJS – TEN.

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2 METHODS

This retrospective descriptive study was conducted in hospitalized patients ofDr. Moewardi General Hospital Surakarta between January 2016 and December 2017. The secondary data were taken from medical record.Datastudy includes the number of SJS - TEN patients, sex, age, comorbid disease, mucosal involvement, culprit drugs, systemic corticosteroid therapy, organ involvement and complications. The data obtained were then analyzed.

3 RESULTS

Table 1. Clinical characteristics and suspected causative agents of cases SJS – TEN January 2016 - December 2017.

	Total (n = 26)	Percentage (%)
Age (year)		
0 – 5	0	0
5 – 11	1	4
12 – 16	0	0
17 – 25	4	15
26 – 35	1	4
36 – 45	5	19
46 – 55	6	23
56 – 65	6	23
>65	3	11
Gender		
Male	15	57
Female	11	42
Diagnosis		
SJS	16	61
SJS overlap NET	5	19
NET	5	19
Comorbid Disease		
Epilepsy	3	11
Diabetes Mellitus	3	11
Stroke	1	4
TBC	2	7
Malignancy	2	7
HIV/AIDS	3	11
CKD	1	4
Hypertension	4	15
Cardiovascular	1	4
Mucosal involvement		
Eye	17	65
Mouth	23	88
Genitalia	3	11
Culprit Drug		
One type	9	34
More than 1 drug	14	53
Not known	3	11
Internal organs involvement		
Hepar	15	57
Kidney	11	43
Antibiotics		
Penicillin	5	19
Cephalosporins	6	23
Clindamycin	2	7
Quinolones	2	7
Anticonvulsants		

Carbamazepine	5	19
Phenytoin	3	11
Valproic Acid	2	7
Non Steroid Anti Inflammatory		
Potassium Diklofenak	1	3
Diclofenac Sodium	2	7
Methampiron	1	3
Mefenamic acid	4	15
Paracetamol	6	23
Ibuprofen	1	3
Antituberculosis drug	2	7
Other drug (benzodiazepines)	1	3

Table 2: The use of systemic steroids in SJS - TENin hospitalized patients of dr. Moewardi General Hospital, January 2016 - December 2017

	Research result
Average treatment duration (days)	10
Number of patients with systemic corticosteroid therapy	26
The average dose of corticosteroid equivalent dexamethasone (mg / day)	25
Average duration of systemic corticosteroid use (days)	10
Total use of corticosteroid therapy over 7 days	12

The averages length of stay (LOS) of SJS - TENpatients was 10 days. All patients received systemic corticosteroid therapy with an average dose of 25 mg per day for 10 days (1.5 mg / kg body weight / day) (Table 2).

4 DISCUSSION

Both SSJ and TEN are rare diseases, with the incidence for SJS 1-6 cases per million inhabitants annually, while TEN 0.4 - 1.2 cases / million / year (Kariosentono, 2015). In this study, during the period of January 2016 - December 2017, 26 patients were hospitalized due to SJS - TEN with the average number of patients was 13 annually. Study by Wanjarus et al reported the average age was 46 years old and women were more affected than men (Roongpisuthipong et al., 2014). These findings are in contrast with our findings in which men were more likely to be affected do than women with the average age of 45 years old. One of the factors that influence the number of SJS -TEN events is genetic factor (Stocka-Łabno et al., 2016).

Research conducted by Stocka-Łabno et al. the most common culprit drug are sulfonamides and anticonvulsants (lamotrigine). In our study the most common culprit drug is antibiotic group cephalosporin and NonSteroid AntiInflammatory paracetamol.

In this study the most involved lesion was in the oral mucosa (88%) followed by eye mucosa (65%) andgenital mucosa (11%). In addition, the manifestation of allergic conditions is not only on the skin and mucosa but also involves internal organs (Venkateshwarlu and Radhika, 2011). Organ involvement in the occurrence of SJS andTEN are 8,1% - 61,5% and 53,8%, respectively (Huang et al., 2009). We found the internal organs involved were liver (57%) and kidney (43%). This occurs because drug mediated hepatitis istoxic whereas abnormal metabolism and hepatocyte damage are the major pathogenic mechanisms. Increased transaminase enzyme is affected by several factors such as inflammatory reactions, fatty liver and viral hepatitis (Huang et al., 2009).

In addition, SJS -TEN patients also partially have comorbid disease. Research conducted by Stocka-Łabno et al. reported that patients with SJS - TEN have comorbid disease such as hypertension. It is the same as our finding that hypertension is the most comorbid disease too.

In SJS -TENpatients require hospitalization to improve the condition (Stocka-Łabno et al., 2016). The length of stay is different depending on the severity of the illness and the accompanying infection (Huang et al., 2009). The average LOS in this study is 10 days, not much different from the research done by Stocka-Łabno et al. 7 days. While research by Haejun et al. has a LOS for 14 days (Yim et al., 2010).

There are no standard guidelines for management SJS-TEN patients. Recognizing and stopping the causative agent are primary (Venkateshwarlu and Radhika, 2011). A retrospective control study conducted in Paris and Germany concluded that corticosteroids did not show any significant effect on mortality but only provided supportive care alone (Kardaun and Jonkman, 2007; Stat et al., 2008). Corticosteroids prevent disease prolongation when administered during the first 72 hours of the initial symptom occurrence. The dose of intravenous dexamethasone (iv) was 1.5 mg / kg / day for 3 consecutive days (Prins, 2012; Valeyrie-Allanore, 2012; Kariosentono, 2015). The use of methylprednisolone iv 500 mg daily (2 days) and 250 mg daily (in the next 3 days) (Kariosentono, 2015). Kim et al. and Hirahara et al. administered methyl prednisolone therapy 250 - 1000 mg / day in NET patients and tapering dose was done gradually with oral prednisone. In our study all SJS -TEN received systemic corticosteroid therapy with a mean duration of corticosteroid tapering dose for 10 days with an average dose equivalent to dexamethasone 25 mg / day or 1.5 mg / kg / body weight.Doses of corticosteroids in SJS -TENpatients at Inpatient Installation of Dr. Moewardi General Hospital is in accordance with therapeutic guidelines. By administering these systemic corticosteroids the patients improved because the mechanism of action is by inhibition of epidermal apoptosis by several mechanisms like IFN-ɣ inhibition that may induce apoptosis and inhibitionapoptosis of Fas.-mediated keratinocyte (Del et al., 2009).

5 CONCLUSION

This retrospective descriptive study was conducted in hospitalized patients of Dr. Moewardi General Hospital Surakarta between January 2016 and December 2017. Treatment of systemic corticosteroids in cases of SSJ-NET in Dr. Moewardi General Hospital Surakarta showed clinical improvement with an average of 10 days treatment and an average dose of 25 mg per day, tappering dose.

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