

# Toxic Epidermal Necrolysis: The Experience of Coimbra's Burn Unit



## Necrólise Epidérmica Tóxica: A Experiência da Unidade de Queimados de Coimbra

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### ABSTRACT

**Introduction:** Toxic Epidermal Necrolysis is a drug-induced life-threatening systemic disease, characterized by extensive dermoepidermal detachment and mucositis. At least 95% of cases are believed to be drug-induced. SCORTEN is a scoring system used to stratify severity and predict mortality. Treatment demands immediate withdrawal of the causative drug and early transfer to a burn centre for specific and intensive care.

**Material and Methods:** Authors have performed a retrospective study of 21 consecutive patients with SJS/ Toxic Epidermal Necrolysis admitted in the Burn Centre of Coimbra's University Hospital, between January 1999 and December 2010, and have compared the actual mortality rate with that predicted by SCORTEN, in order to assess the predictive capacity of SCORTEN. Analysis of results and treatment options were conducted. Data were analysed in SPSS 17.0®.

**Results:** Thirteen females (61.9%) and 8 males (38.1%) were treated, mean age  $55.6 \pm 23.7$  years and with a mean of  $51\% \pm 22.4\%$  epidermal detachment. The overall observed mortality rate was 47.6% and the one predicted by SCORTEN 42.2%. Immediate withdrawal of the causative drug and early transfer of the patient to our burn centre were the basis of treatment.

**Conclusion:** Toxic Epidermal Necrolysis pathophysiology remains to be clarified and no specific treatment has unequivocally proven to be effective. SCORTEN seems to be an accurate scoring system for estimation of mortality rate.

**Keywords:** Burns; Burns Units; Epidermal Necrolysis, Toxic; Predictive Value of Tests; Severity of Illness Index.

### RESUMO

**Introdução:** A necrólise epidérmica tóxica é uma doença sistémica grave, potencialmente fatal, caracterizada por febre, descolamento dermoepidérmico extenso e erosão das mucosas. Em 95% dos casos, consiste numa reacção idiosincrática à administração de fármacos. A gravidade da doença é estratificada através da aplicação de uma escala de previsão da mortalidade, denominada SCORTEN. O tratamento obriga à suspensão imediata do fármaco suspeito e à referenciação do doente a uma Unidade de Queimados capaz de assegurar um tratamento específico.

**Material e Métodos:** Estudo retrospectivo de 21 doentes internados com SJS/ Necrólise Epidérmica Tóxica na Unidade de Queimados dos Hospitais da Universidade de Coimbra, entre Janeiro de 1999 e Dezembro de 2010 com avaliação dos resultados e das opções terapêuticas. Comparação das taxas de mortalidade desses doentes com as previstas pelo SCORTEN, no sentido de avaliar a capacidade preditiva desta escala. Os dados foram analisados no programa SPSS 17.0®.

**Resultados:** Foram internados 13 doentes do sexo feminino (61,9%) e 8 do sexo masculino (38,1%), com média de idades de  $55,6 \pm 23,7$  anos e com  $51\% \pm 22,4\%$  de superfície corporal atingida. A taxa de mortalidade dos doentes internados foi de 47,6% e a prevista pelo SCORTEN foi de 42,2%. O tratamento instituído centrou-se na remoção imediata do fármaco suspeito e na referenciação precoce do doente para a unidade.

**Conclusão:** A fisiopatologia da necrólise epidérmica tóxica não está completamente esclarecida, pelo que não existe actualmente uma terapêutica específica, comprovadamente eficaz. A utilização do SCORTEN permite uma previsão adequada da taxa de mortalidade nestes doentes.

**Palavras-Chave:** Necrólise Epidérmica Tóxica; Queimaduras; Unidades de Queimados; Índice de Gravidade de Doença.

### INTRODUCTION

Toxic epidermal necrolysis (TEN) is a rare, life-threatening disease characterized by hyperthermia, painful and extensive dermoepidermal exfoliation and mucosal erosions.<sup>1</sup> Mucosal involvement can lead to the appearance of ophthalmologic and genito-urinary complications, as well as to respiratory failure and gastro-intestinal bleeding.

In 95% of cases, it is recognized to be an idiosyncratic reaction to the administration of certain type of drugs, notably to anticonvulsants, allopurinol, sulfonamides, non-steroidal anti-inflammatory drugs, among others,<sup>2</sup> comprising 1% of all hospital admissions related to adverse drug

reactions.

The yearly incidence of TEN reaches about 0.4 to 1.3 per million individuals in Western populations.<sup>3,4</sup> Mortality rate is estimated to be 30% to 50%, being mainly due to sepsis and multiorgan failure.<sup>3</sup>

Studies seem to indicate that epidermolysis is due to keratinocyte apoptosis (mediated by Fas-FasL and perforin-granzyme B systems) triggered by themselves in the presence of a specific drug or metabolite, which is amplified by inflammatory cells (particularly CD8<sup>+</sup> T lymphocytes) and inflammatory soluble mediators, leading to keratinocyte ne-

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crisis and massive epidermal destruction.<sup>5</sup>

Accordingly to Bastuji-Garin et al,<sup>6</sup> Stevens-Johnson syndrome (SJS) and TEN are considered to be on opposite sides of essentially the same disease, being differentiated only by the extent of total body surface area (TBSA) involved. In SJS, epidermal loss affects less than 10% of TBSA, in TEN the involvement is higher than 30%, being the rest of the cases classified as SJS/TEN overlap. Clinically, SJS and TEN are characterized initially by flu-like symptoms, which are followed in the next days by rapid and extensive dermoepidermal detachment and erosion of mucous membranes, the latest considered as an important clue to diagnosis. Skin involvement begins as painful purpuric macules with necrotic centers or atypical target lesions with centrifugal distribution that tend to coalesce to form flaccid blisters and evolve to diffuse epidermal detachment with a positive Nikolsky sign (easy removal of non-detached areas by finger pressure).<sup>7</sup>

SCORTEN<sup>8</sup> (severity-of-illness score for TEN) is a prognostic scoring system used to predict disease severity and patient outcome from TEN, based on seven clinical and laboratorial variables present during the first 24 hours of admission. Its use among patients admitted in Burn Centers has been questioned by many authors, since these burn units usually treat the most aggressive forms of the disease and SCORTEN was initially designed to be applied to the whole spectrum of SJS-TEN patients.<sup>9</sup>

Since TEN pathophysiology remains to be clarified no specific treatment has unequivocally proven to be effective. It has been demonstrated that immediate suspension of the offending drug and all non-essential medications as well as early transfer of the patient to a Burn Centre are associated to lower mortality rates.<sup>7</sup> Supportive therapy includes fluid and electrolyte balance, infection prevention and thermoregulation, similarly to the treatment of a burned patient, in order to promote rapid reepidermization of denuded areas.

This study was conducted to review the SJS, SJS/TEN and TEN patients admitted to the Burn Unit of the University Hospitals of Coimbra, Portugal, over a period of twelve years (1999 to 2010) as well as to analyse the results and treatment options in these patients. In addition, the authors propose to assess the predictive capacity of SCORTEN based on this sample.

## MATERIAL AND METHODS

### Data Collection

During the period from January 1999 to December 2010 all patients admitted to the Burns Unit of the University Hospitals of Coimbra (HUC) with the diagnosis of SJS, SJS/TEN or TEN were included in the study. Through a retrospective chart, the authors reviewed clinical and laboratory data present in medical files of twenty-one patients. Cases were excluded if any of the variables used to determine SCORTEN in the first 24 hours of admission (age, presence of malignancy, % TBSA of detached epidermis, peak heart rate and serum blood urea nitrogen, glucose and bicarbo-

nate levels) were omitted in the medical files. In addition to these variables, collected data included gender, length of hospital stay, probable causative agent, time interval between first symptoms and referral as well as time interval between beginning of the disease and withdrawal of the suspected drug. Relevant comorbidities, previous therapy with corticosteroids, mucosal involvement, acute complications (namely, pneumoniae and sepsis), modality treatments and outcome were also registered. Based on laboratory records, authors studied the microbiological profile of patients who sustained pneumoniae during hospitalization. TEN diagnosis was made through cutaneous biopsy, whenever possible, or through clinical criteria. Sepsis was considered whenever signs of SIRS (temperature greater than 38.5 °C or less than 35 °C, heart rate greater than 90 beats/min, respiratory rate greater than 20 breaths/min or PaCO<sub>2</sub> less than 32 mmHG, white blood count greater than 12000 cells/mm<sup>3</sup> or less than 4000 cells/mm<sup>3</sup> or relative count of immature forms greater than 10%) were present associated with infection confirmed by positive cultures. In order to assess the accuracy of SCORTEN, mortality rate was calculated among the population in study and compared with the mortality rate predicted by SCORTEN. Statistical analyses were performed using SPSS for Windows version 17.0 applying unpaired two-tailed student's *t*-tests and  $\chi^2$  as appropriate. A *p* value < 0.05 was considered significant.

### Treatment Protocol

After investigating recent exposure to drugs, all non-essential medications, probable causative drug as well as antibiotics which have been previously introduced were immediately suspended. Corticosteroids instituted before admission were either stopped acutely or tapered. Percentage of TBSA of detached epidermis was estimated using Lund and Browder charts and fluid needs were calculated accordingly with Parkland's formula and replaced with crystalloids (Ringer's lactate). Since fluid requirements in these patients are usually less than in burn patients, the initial infusion rate, despite of being estimated through Parkland's formula, was carefully titrated based on urinary output and clinical response of the patient. Other intensive care attitudes were used as needed, namely hemodynamic and respiratory support, enteric nutrition and supplementation with glutamine and other immunomodulatory nutrients. In order to prevent infection, patients were treated in isolation rooms with strict aseptic techniques. At admission, areas of loose epidermal patches and mucosal plaques were removed under sedation and disinfected with chlorhexidine solution, which was repeated daily until no more epidermal detachment was observed. Raw areas were dressed with Omiderm<sup>®</sup> or nanocrystalline silver impregnated systems. Analgesia was given regularly, mainly with opioids. Antibiotic therapy was only initiated when first signs of sepsis occurred. Broad spectrum antibiotics were initially chosen and posteriorly adapted accordingly to the antibiogram. Since 2006, date of enforcement of the present protocol, intravenous high doses of N-acetylcysteine (2 g/d), intra-

venous immunoglobulin (1 g/Kg/d for 3 days) and plasmapheresis (usually 3 sessions) were initiated on admission in all patients. Daily observation by an ophthalmologist to prevent ophthalmological complications was the rule. Daily clinical analyses and sampling for bacteriological cultures (skin, blood, urine and bronchial aspirates/sputum) and antibiogram three times a week were performed in all critical ill patients.

## RESULTS

Table 1 summarizes clinical and demographic characteristics and outcome of all patients included in the study. During the period in study, 21 patients were admitted for SJS/TEN or TEN in our Burns Center, 13 female (61.9%) and 8 male (38.1%) with a mean age of  $55.6 \pm 23.7$  years (range 14 - 91 years) and a mean of  $50.5 \pm 22.5\%$  TBSA epidermal detachment. In 4 patients (19%), SJS/TEN was the clinical diagnosis whereas TEN was present in 17 patients (81%). None of the admissions in the study group corresponded to SJS.

Mean time interval between first symptoms and referral to our Burns Unit was  $5.3 \pm 4.9$  days and time interval between beginning and withdrawal of the suspected drug was  $9.2 \pm 10.5$  days (it was not possible to quantify this interval in 5 patients due to lack of information in medical files). Mean length of hospital stay among the survivors was  $13.5 \pm 7.2$  days.

The most frequently encountered causative drugs were beta-lactam antibiotics (23.8%) followed by allopurinol (19%). In the rest of the patients, the suspected agents were anticonvulsants (phenytoin and lamotrigine), paracetamol, antibiotics (cotrimoxazol, meropenem and azithromycin) and NSAIDs (diclofenac). In 3 patients (14.3%) the offending drug wasn't identified.

Mucosal involvement was present in all patients and affected most frequently buccal mucosa ( $n = 18$ ). Fig. 1 shows distribution of mucosal involvement.

Relevant comorbidities were present in 17 patients. Eleven (52.4%) had medical history of cardiovascular diseases, namely hypertension and coronary disease, and metabolic disorders such as Diabetes Mellitus and dyslipidemia were present in 6 patients (28.6%). Other comorbidities identified included neurological diseases ( $n = 5$ ); autoimmune disorders ( $n = 5$ ) such psoriasis, myasthenia gravis and rheumatoid arthritis; malignancy ( $n = 3$ ) namely breast cancer, lymphoma and cerebral tumor; chronic infectious diseases ( $n = 2$ ); chronic renal failure ( $n = 2$ ) and depression syndrome ( $n = 1$ ) – Fig. 2.

Data collection concerning previous treatment with corticosteroids prescribed by general practitioners or in referring hospitals show that this type of drugs was used in 13 patients (61.9%).

Pneumonia was the most prevalent acute complication (42.9%) during hospitalization obliging to ventilator support in 44.4% of cases. Microbiologic evaluation of sputum or bronchial aspirate samples showed MRSA (methicillin-resistant *Staphylococcus aureus*) in 33.3%, *Candida albicans*

in 11.1% and several Gram-negative species in the rest of the patients. Sepsis occurred in 19% of patients.

In terms of treatment modalities, 16 patients (76.2%) were treated with N-acetylcysteine and 11 patients (52.4%) with intravenous immunoglobulin (IVIG). Plasmapheresis was used in 10 patients (47.6%) as two or three sessions. Survival rate among the group of 5 patients who have not received any of these treatments was lower (40%) as compared with the group of 6 patients who have been treated with these three pharmacologic agents (66.7%), although without statistically significant difference ( $p = 0.567$ ).

With regard to long-term sequelae, 4 patients developed long-term cutaneous complications, namely pigmentation abnormalities ( $n = 3$ ), chronic pruritus ( $n = 2$ ) and ungueal dystrophy ( $n = 1$ ). Of the 17 patients with ocular involvement, one had symblepharon formation associated with photophobia and xerophthalmia and another one had epiphora and cilia depletion. One patient developed labia majora synechia.

The mean SCORTEN score was  $3.2 \pm 1.1$  (range 2-5). Table 1 summarizes the number of patients and deaths for each SCORTEN level as well as the comparisons between real and predicted mortality rates. There was no statistically significant difference between the overall mortality rate of 47.6% (10 patients) in the population in study and the overall mortality rate of 42.2% (8.9 patients) predicted by SCORTEN ( $P = 0.142$ ) – Table 2.

Comparison between nonsurvivors and survivors concerning age, time interval between first symptoms and referral to burn unit and duration of treatment with the suspected drug showed that the former group had a trend towards highest age ( $64.4 \pm 23.6$  years vs.  $47.6 \pm 21.7$  years;  $P = 0.104$ ), longer time interval between first lesions and referral to the Burns Center ( $6 \pm 5.8$  days vs.  $4.7 \pm 4.2$  days;  $p = 0.57$ ) and towards wider treatment duration with the causative drug ( $11 \pm 10.8$  days vs.  $6.9 \pm 10.4$  days;  $p = 0.45$ ).

## DISCUSSION

In Portugal, data concerning treatment of SJS and TEN patients in Burn Units are very scarce and the present retrospective study corresponds to the largest series of patients admitted in a Burn Center due to these exfoliating diseases in our country.<sup>10-12</sup> Since SJS/TEN are rare conditions, our sample size is limited but similar to other international series published in literature.<sup>13-15</sup>

TEN can affect people of all ages and all ethnicities, but is recognized to be more frequent at extreme ages. In our group of patients the mean age (55.6 years) was equivalent or slightly higher to other studies,<sup>12-14,16</sup> but is important to state that, in opposite to other centers, admissions in our burn unit are restricted to patients older than 12 years old. We have observed a preponderance of cases in the female gender, which is also in agreement with literature<sup>4,17</sup> and recent studies.<sup>13-15</sup>

In the majority of patients the final diagnosis was TEN (81%), reflecting the greater severity of patients who are

Table 1 - Patient characteristics

Patient	Age (years)	Length of burns unit admission (days)	Days between initial symptoms and referral	Days of exposure to the probable offending drug	Probable causative drug	SCORTEN	TBSA (%)	Plasma-pheresis	IVIg	Acetylcysteine	Pneumonia	Sepsis	Outcome
1	79	4	7	?	?	2	80						Survived
2	81	2	21	20	Paracetamol	5	44						Died
3	37	3	7	2	$\beta$ -lactam	4	21				+	+	Survived
4	14	2	5	35	Lamotrigine	2	50						Died
5	63	10	4	4	$\beta$ -lactam	3	80						Died
6	80	9	15	?	$\beta$ -lactam	4	93		+	+	+		Survived
7	67	1	2	5	Allopurinol	4	100			+	+	+	Died
8	84	10	7	7	Allopurinol	3	50		+	+	+		Died
9	34	8	1	3	Meropenem	2	17.5		+	+	+		Survived
10	91	9	8	?	?	4	25		+	+	+		Died
11	50	3	6	16	Cotrimoxazol	5	38		+	+	+		Died
12	64	23	2	?	?	4	45	+		+			Survived
13	16	25	2	4	Paracetamol	2	46	+		+			Survived
14	15	16	6	?	Azithromycin	2	45	+		+			Survived
15	64	4	1	3	$\beta$ -lactam	5	24	+		+		+	Died
16	51	14	1	1	Phenytoin	4	35	+	+	+			Survived
17	53	14	6	1	Allopurinol	3	60	+	+	+			Survived
18	44	4	5	2	Diclofenac	2	37	+	+	+			Died
19	86	8	1	7	$\beta$ -lactam	4	45	+	+	+	+	+	Died
20	49	18	3	7	Phenytoin	2	61	+	+	+	+		Survived
21	45	14	2	30	Allopurinol	2	30	+	+	+			Survived

Table 2 - Number of patients and comparison between real and predicted mortality rates for each SCORTEN level

SCORTEN	Number of patients	Predicted mortality (No. of deaths)	Real mortality (No of deaths)
0	0	1.2%	–
1	0	3.9%	–
2	8	12.2% (1)	25% (2)
3	3	32.4% (1)	66.7% (2)
4	7	62.2% (4.3)	42.9% (3)
5	3	85% (2.6)	100% (3)
6	0	95.1%	–
7	0	98.5%	–
Total	21	42.2% (8.9)	47.6% (10)

usually admitted in burn centers, being the less severe forms of these spectrum of diseases treated in other hospital departments (like Dermatology departments). Comparing with recent studies, we have a much higher proportion of patients with TEN which is also consonant with high TBSA epidermal detachment values (50.5%) observed in our patients. In fact, a review of 61 patients at a Canadian burn unit<sup>16</sup> found 54% of TEN as the final diagnosis, almost 30% lower than in our study.

Most researchers consider TEN as an idiosyncratic drug reaction in 95% of cases.<sup>2</sup> In our study, we found that 18 cases (86%) could be attributed to a single drug based on clinical and chronological criteria, in agreement with literature. Antibiotics, mainly beta-lactams, were the agents most frequently involved in this series, followed by allopurinol, as also noted by two other study groups from Birmingham's University Hospital<sup>14</sup> and Sydney's General Hospital.<sup>18</sup> However the EuroSCAR study,<sup>19</sup> a prospective case-control study conducted in six countries (Austria, France, Germany, Israel, Italy and Netherlands), has identified allopurinol as the most common cause of SJS and TEN, particularly when administered in high doses.

Admission delay in our burn unit was 5.3 days (range 1-21), almost twice than in other studies,<sup>13,14</sup> corresponding to a very late referral and thus a delayed start of optimal supportive and therapeutic care, even though most of them have been transferred from another hospital department besides the Emergency Room. In addition, suspension of the causative drug was also belated (9.2 days; range 1-35). Together, these two points can reflect a delayed diagnosis due to lack of awareness among physicians for this type of pathologies, attending to their rarity and unspecific initial clinical features, turning educational campaigns of greatest importance. In literature,<sup>7</sup> besides high SCORTEN values, late transfer to a specialized center as well as delayed identification and withdrawal of the provocative agent have been associated with poor outcomes and higher mortality rates.

It has also been reported that early elimination of the causative drug may reduce the risk of death by 30% per day.<sup>7</sup> Indeed, when analyzing our results concerning time interval between onset of symptoms and referral to our burn unit and duration of treatment with the suspected drug, non-survivors had a trend towards wider time intervals ( $p = 0.57$ ;  $p = 0.45$  respectively).

Clinically, mucosal involvement was present in all patients with simultaneous commitment of different mucosal membranes in the majority of cases. In fact, it is well known that mucosal involvement occurs in more than 90% of patients, usually preceding skin lesions in 1 to 3 days, displaying a special tropism for stratified squamous epithelium and affecting most often buccal, ocular and genital mucosa.<sup>4</sup> Association of typical skin lesions and mucosal erosions are an important clue to early diagnosis, particularly in presence of ocular involvement.

Sepsis and multiorgan failure are the two major causes of death in TEN, the former being responsible for 50% of deaths in the acute phase of the disease.<sup>3</sup> This high incidence of sepsis is related to loss of skin barrier with consequent tissue invasion by endogenous flora as well as by exogenous microorganisms, which multiply exponentially in the exudate and necrotic tissues. It is also dependent of the very frequent use of central venous catheters in these patients. Sepsis can also result from pneumonia. Indeed, respiratory mucosa involvement is observed in 27% of patients, with intubation and mechanical ventilation support in 10 to 20% of cases.<sup>20</sup> Increased alveolocapillary permeability with secondary pulmonary edema, polypnea due to pain and aspiration of debris from oropharyngeal and tracheobronchial mucosa detachment can lead to atelectasias, bronchial pneumonia and, in more severe cases, to ARDS (*adult respiratory distress syndrome*). In agreement with these data and with other studies,<sup>12-14</sup> infectious complications, like pneumonia and sepsis, were frequent in our group of patients. Pneumonia was a major cause of morbid-

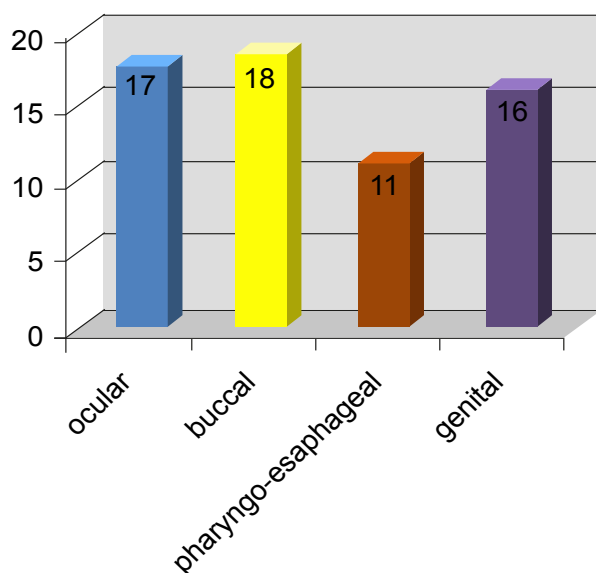


Figure 1 - Distribution of mucosal involvement in the study group.

ity during hospitalization and MRSA appeared as the principal microorganism cultured, probably related to the high incidence of this pathogen in skin flora.

As we described previously, corticosteroids instituted before admission were either stopped acutely or tapered ( $n = 13$  patients). The role of corticosteroids in TEN remains controversial. Several retrospective studies<sup>21-23</sup> have shown enhanced mortality (up to 12.5 times), delayed skin lesions healing, prolonged hospital stay and higher infectious rates (up to 5 times) in patients treated with systemic corticosteroids. In addition, case reports of patients who developed TEN while being on treatment with corticosteroids for other comorbidities have been described, suggesting that corticosteroids do not prevent development of disease. Nevertheless, van der Meer et al<sup>24</sup> and Kardaun et al<sup>25</sup> have suggested that high doses of corticosteroids administered as pulses and in an early phase of disease reduce significantly death risk. In conclusion, recent data seems to indi-

cate that corticosteroids could be useful in the erythrodermic stage, before dermoepidermal detachment. Administration beyond the initial 48 hours of disease is associated with higher morbidity and mortality rates.<sup>26</sup> Since TEN diagnosis in non-bullous phase is rare and difficult, early treatment with corticosteroids rarely takes place. According to these data and as all patients presented already epidermal detachment at admission in our burn unit, our policy was to suspend corticosteroids.

Plasmapheresis has been used in many centers with promising results as concluded by some retrospective reports, showing survival rates between 77% and 100%.<sup>27-29</sup> Its proponents believe that it removes the causative drug or its metabolites and soluble inflammatory mediators from the bloodstream. The opponents argue that it may also eliminate anti-inflammatory mediators and, attending to the short half-life of cytokines, it will probably be instituted too late, limiting its value.

Several meta-analyses, retrospective and prospective studies have been published in the last years in order to understand the role of IVIG in the treatment of SJS/TEN patients, with contradictory results concerning morbidity and mortality, probably related to wide variation in treatment protocols and in anti-Fas activity among different batches.<sup>30-34</sup> Despite these contradictions and although controlled and randomized studies have not been published yet, the majority seems to indicate a benefit in mortality rates with early administration of high IVIG doses (1g/Kg/day, during 4 days, in continuous infusion).

Other immunomodulatory drugs like N-acetylcysteine, cyclosporin A, pentoxifylline, granulocyte colony-stimulating factor, anti-TNF- $\alpha$  antibodies, cyclophosphamide and ulinastatin are being used in multiple units, in spite of lack of clear evidence of a beneficial role in the management of these patients.<sup>5</sup>

Since none of the mentioned specific treatments have proven to be completely effective or even superior to supportive care, immediate withdrawal of the causative drug and early transfer to a Burn centre in order to prevent infec-

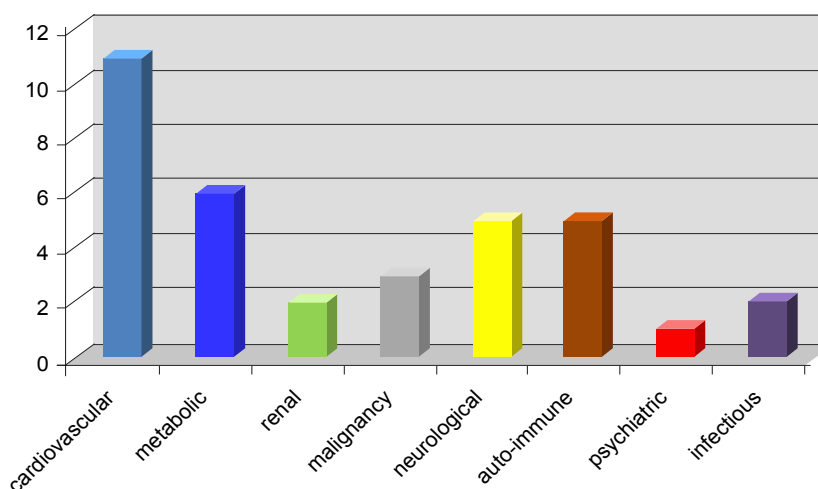


Figure 2 - Comorbidities present in the study group

tion, hydroelectrolytic changes and to promote rapid reepithelization of denuded areas are the mainstream attitudes with confirmed benefits and impact in SJS/TEN morbidity and mortality. Burn centers are therefore recognized to be best suited to care SJS/TEN patients, attending to their expertise in treating large denuded skin areas in critically ill patients.<sup>35</sup>

SCORTEN is a scoring system developed by Bastuji-Garin *et al* which is used to stratify gravity and estimate mortality.<sup>8</sup> Its application in TEN patients treated in burn units has been called into question by some authors who argue that SCORTEN overestimates mortality, since it was initially endorsed from a group with less severe forms of the disease.<sup>9</sup> In our sample we found a good correlation between predicted and actual mortality which supports the accuracy of SCORTEN in predicting SJS/TEN mortality, as already established in other studies.<sup>12,14,16</sup>

The mortality rate in our group of patients was high (47.6%), but still consistent with literature.<sup>3,12,36</sup> Several features present in our sample may contribute to this high mortality rate namely higher proportion of patients with TEN, high mean TBSA involvement and mean age, high percentage of comorbidities and late transfer of the patient to our unit as well as late withdrawal of the culprit drug.

Our study was designed as a retrospective analysis, with all the limitations inherent to this type of study, namely

in data collection. Besides, it was not possible to compare the real impact of specific therapeutic modalities in survival rates and to prove or disprove newer treatment protocols for TEN.

Since it is a rare disease, sample size was small which also restricts statistical data analyses and conclusions in some way.

## CONCLUSION

Since SJS/TEN's pathophysiology is still not completely clarified, a specific and efficient treatment hasn't been yet identified. Nowadays, early diagnosis, immediate referral to a burn unit in order to provide a specific and intensive treatment and suspension of the causative drug are the pillars of treatment of these exfoliating disorders. Therefore, educational campaigns assume greatest importance in order to alert physicians to these diseases.

Finally, SCORTEN seems to be an accurate method to predict mortality rate in SJS/TEN patients.

## CONFLICT OF INTERESTS

None stated.

## FUNDING SOURCES

None stated

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