Scratching the Surface: A Review of SJS/TEN

Sarah Smith, PharmD

Pharmacy Grand Rounds 2018
November 27, 2018
Stevens-Johnson Syndrome

Toxic Epidermal Necrolysis

Did you know there are 7 types of dermatological emergencies?

Rocky Mountain Spotted Fever

Necrotizing Fasciitis

Cutaneous Anthrax

Meningococcemia

Toxic Shock Syndrome
Objectives

1. Review the pathophysiology of Stevens-Johnson syndrome (SJS) and Toxic epidermal necrolysis (TEN)

2. Identify medications that may induce SJS/TEN

3. Discuss pharmacological interventions used to treat patients who present with SJS/TEN
Abbreviations

• SJS: Stevens-Johnson syndrome
• TEN: Toxic epidermal necrolysis
• CBZ: carbamazepine
• APC: antigen presenting cell
• IVIG: intravenous immune globulin
• FasL: Fas ligand

• sFasL: soluble Fas ligand
• TNF-α: Tumor necrosis factor-alpha
• RCT: randomized control trial
• CTL: cytotoxic T lymphocytes
• SCARs: severe cutaneous adverse reactions
Patient Case

• 38 year old male

• PMH: epileptic seizures
  • Developed high fever, sloughing of the epidermis, and clinical appearance of severe burn patient 2 weeks after starting a new antiepileptic medication
SJS/TEN

- Acute, life-threatening hypersensitivity cutaneous reactions
- Characterized by full-thickness epidermal necrosis
- Varying involvement of cutaneous, extracutaneous, and mucous membrane involvement
Distinguishing SJS vs TEN

- SJS
- SJS/TEN overlap
- TEN

Percentage of BSA affected

- ≤10% BSA
- 10-30% BSA
- >30% BSA


Clinical Course of SJS/TEN

Prodrome:
malaise, rash, fever, cough, myalgia
• 1-4 weeks after drug exposure

Epidermal detachment progresses, large denuded areas
• Extreme pain, massive fluid & protein loss, hypothermia

1 3 5 7
days

Signs begin in mucous membranes
Skin lesions start to manifest, progress to large blisters

Re-epithelialization of the epidermis begins
• May take up to 3 weeks

Clinical Presentation

**Extracutaneous**

**Nonspecific:**
- Malaise, rash, fever, pain, cough, headache, N/V

**Respiratory**
- Large ulcerations and epithelial necrosis of bronchial epithelium, respiratory distress, pulmonary edema, progressive respiratory failure

**Gastrointestinal**
- Diarrhea, nausea, malabsorption, colonic perforation, melena

**Renal**
- Proteinuric, hematuric, microalbuminuria
Clinical Presentation

Cutaneous

**Initial Phase:**
- Erythematous, dusky red, flat atypical target lesions with necrotic centers
- Lesions evenly distributed on face/trunk/proximal part of limbs

**Later phase:**
- Lesions coalesce and evolve into flaccid blisters
- Epidermal detachment
- + Nikolsky sign
  - Gentle lateral pressure causes lesional, detachable epidermis

Adapted from JAMA 2017; 153 (12): 1344
Clinical Presentation

Mucous membrane

Ocular:
- Eyelid edema, redness, photophobia, discharge, lacrimation

Buccal/Oral:
- Erosive, hemorrhagic lesions, grayish-white pseudomembranes, crust on lips, nose involvement

Genital
- Erosive hemorrhagic lesions, painful urination

Adapted from JAMA 2017; 153 (12): 1344
Epidemiology

- US incidence:
  - 2.9-6.1 cases per 1 million people per year
  - 1,178 cases reported to the FDA in 2017

- More common in women
  - Female to male ratio of 1.5:1


Four severe adverse events and the leading suspect drugs. *ISMP Medication Safety Alert! Acute Care.* 2018; 23 (18).
Mortality

• Mortality estimates:
  • SJS: 1 – 12.5%
  • SJS/TEN overlap: 19.4%
  • TEN: 15 – 50%

• SCORTEN criteria
  • Severity of illness score to predict mortality for SJS/TEN
  • Measure on days 1 & 3 of hospitalization
SCORTEN criteria

- Age >40 years
- Malignancy
- BSA >10%
- Heart rate >120 bpm
- BUN >28 mg/dL
- Serum glucose >250 mg/dL
- Serum bicarbonate <20 mmol/L

1 point for each risk factor present

<table>
<thead>
<tr>
<th># Risk Factors</th>
<th>Predicted Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1%</td>
</tr>
<tr>
<td>1</td>
<td>4%</td>
</tr>
<tr>
<td>2</td>
<td>12%</td>
</tr>
<tr>
<td>3</td>
<td>32%</td>
</tr>
<tr>
<td>4</td>
<td>62%</td>
</tr>
<tr>
<td>5</td>
<td>85%</td>
</tr>
<tr>
<td>6</td>
<td>95%</td>
</tr>
<tr>
<td>7</td>
<td>99%</td>
</tr>
</tbody>
</table>


Patient Case

• 38 year old male
• PMH: epileptic seizures
  • Developed high fever, sloughing of the epidermis, and clinical appearance of severe burn patient 2 weeks after starting a new antiepileptic medication
Patient Case

- 80% BSA involvement
- Lab values
  - HR: 132 bpm
  - BUN: 36 mg/dL
  - Serum creatinine: 1.2 mg/dL
  - Glucose: 186 mg/dL
  - Bicarbonate: 28 mmol/L
How would you classify this patient?

a) SJS
b) SJS/TEN overlap
c) TEN
How would you classify this patient?

a) SJS
b) SJS/TEN overlap
c) TEN
Etiology

• Known causes:
  • Drugs
    • Most common
    • 50% of SJS cases; 80-90% of TEN cases
  • Vaccinations
    • MMR, varicella, tetanus, influenza, hantavirus (HFRS)
  • Sunlight exposure
  • Pregnancy

Etiology

• Known causes:
  • Infectious agents
    • Herpes virus, *Mycoplasma pneumoniae*, HIV, Hepatitis A
  • Noninfectious conditions:
    • Cancer, radiation, lupus erythematosus, collagen vascular disease
  • Bone marrow/solid organ transplants
  • Idiopathic

Genetic Factors

**HLA-B*15:02**
- Carbamazepine-, lamotrigine-, oxcarbazepine-, & phenytoin-related SJS/TEN
- Asian ancestry

**HLA-B*58:01**
- Allopurinol-related SJS/TEN
- Asian & Non-Asian populations

**HLA-A*31:01**
- Carbamazepine-related SJS/TEN
- Japanese, Indian, & European ancestry

Other possible associations: HLA-B*15:08, HLA-B*15:11, HLA-B*15:18 & HLA-B*51:01
## SJS/TEN Inducing Medications

### Most Common Agents
- Allopurinol
- Carbamazepine
- Lamotrigine
- Nevirapine
- Oxicam NSAIDs
- Phenobarbital
- Phenytoin
- Sulfamethoxazole and other sulfur antibiotics
- Sulfasalazine

### Other Suspected Agents
- **Antibiotics:** Aminopenicillins, Cephalosporins, Quinolones, Tetracyclines, Macrolides
- Valproic acid
- Oxcarbazepine
- Abacavir
- Diclofenac
- Zonisamide
- Lenalidomide
- Acetazolamide
- Ethambutol
- Mirtazapine
- Oseltamivir

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Drug-Induced SJS/TEN

• Most often occurs within 4-28 days of 1st exposure to suspect drug

• May also occur:
  • Within hours upon rechallenge
  • Up to 8 weeks post-exposure

• ALDEN (ALgorithm of Drug causality for Epidermal Necrolysis)
  • Assessment tool for drug causality in SJS/TEN
Pathophysiology

- SJS/TEN characterized by:
  - Apoptotic keratinocyte cell death in the epidermis
  - Epidermal detachment and necrosis
- Exact pathogenesis unknown
One Proposed Theory of Pathogenesis:

CBZ + protein → APC → CBZ + protein → APC → T cell

keratinocyte apoptosis

release of cytokines

Granulysin, sFasL, Perforin, Granzyme B

CBZ = carbamazepine, APC = antigen presenting cell, sFasL = soluble Fas ligand


Complications

- Secondary skin infections
- Bloodstream infections
- Eye problems
- Persistent respiratory sequelae
- Permanent skin damage
  - Abnormal bumps, coloring, possible scarring
  - Hair loss, nail deformities

Patient Case

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• PMH: epileptic seizures
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Patient Case

• 80% BSA involvement

• Lab values
  • HR: 132 bpm
  • BUN: 36 mg/dL
  • Glucose: 186 mg/dL
  • Bicarbonate: 28 mmol/L
What medication most likely caused this patient’s reaction?

a) Lamotrigine
b) Valproic acid
c) Oxcarbazepine
What medication most likely caused this patient’s reaction?

a) Lamotrigine
b) Valproic acid
c) Oxcarbazepine
Early drug withdrawal
Transfer to burn ICU
Room temp 30-32°C
Calculate SCORTEN
• Days 1 & 3
Consider adjuvant therapies
• Within 24-48 h
Supportive care
Consult specialties
• Dermatology
• Ophthalmology
• Urology

No formal US Guidelines available

# Supportive Care

## Pain Control
- No current guidelines
- PCAs may be difficult due to hand involvement
- Avoid morphine when able

## Fluids
- Aggressive fluid & electrolyte replacement
- Maintain urine output 0.5-1 mL/kg/h

## Antibiotics
- *Only* if infection is present
- May lead to drug resistance
- Potential to worsen skin toxicity

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**Citations**

Supportive Care

### Eye Care
- Eye emollients
- Antiseptic eye drops
- Topical antibiotics
- Topical steroids
- Severe cases: amniotic membrane transplantation

### Wound Care
- Disinfecting mouthwashes (chlorhexidine)
- Mild ointments (white petrolatum)
- Avoid topical anti-infectives with a sulfa-moiety

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Treatment

Consider adjuvant therapies

• Systemic corticosteroids
• IVIG
• Cyclosporine
• Infliximab
• Etanercept
• Plasmapheresis
Corticosteroids

Proposed mechanism:

- Ability to modify inflammatory and immune responses
## Corticosteroids

<table>
<thead>
<tr>
<th>Author &amp; year</th>
<th>Study type</th>
<th>Number patients</th>
<th>Treatment</th>
<th>Mortality with/without steroids</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Halebian et al. 1987&lt;sup&gt;1&lt;/sup&gt;</td>
<td>Retrospective comparative trial</td>
<td>30</td>
<td>Hydrocortisone 240-1,000 mg over max 7 days</td>
<td>66% / 33%</td>
<td></td>
</tr>
<tr>
<td>Kelemen et al. 1995&lt;sup&gt;2&lt;/sup&gt;</td>
<td>Retrospective</td>
<td>51</td>
<td>NR</td>
<td>50% / 3%</td>
<td>Infection, hospitalization, &amp; mortality reduced if &lt;48 h steroids</td>
</tr>
<tr>
<td>Kakourou et al. 1997&lt;sup&gt;3&lt;/sup&gt;</td>
<td>Retrospective</td>
<td>16</td>
<td>Methylprednisolone 4 mg/kg/day</td>
<td>0% / 0%</td>
<td>Shorter period of fever with steroids</td>
</tr>
<tr>
<td>Forman et al. 2002&lt;sup&gt;4&lt;/sup&gt;</td>
<td>Retrospective</td>
<td>39</td>
<td>NR</td>
<td>3.6% / -</td>
<td>21% complications</td>
</tr>
<tr>
<td>Kardaun and Jonkman 2007&lt;sup&gt;5&lt;/sup&gt;</td>
<td>Retrospective</td>
<td>12</td>
<td>Dexamethasone 100 mg or 1.5 mg/kg x 3 days</td>
<td>8.3% / -</td>
<td></td>
</tr>
<tr>
<td>Yamane et al. 2007&lt;sup&gt;6&lt;/sup&gt;</td>
<td>Retrospective</td>
<td>117</td>
<td>Prednisolone 10-600 mg/day</td>
<td>3.6% / 16.6%</td>
<td></td>
</tr>
<tr>
<td>Schneck et al. 2008&lt;sup&gt;7&lt;/sup&gt;</td>
<td>Retrospective multicenter</td>
<td>281</td>
<td>NR</td>
<td>17.6% / 27.8%</td>
<td>No significant benefit to any treatment</td>
</tr>
<tr>
<td>Yang et al. 2009&lt;sup&gt;8&lt;/sup&gt;</td>
<td>Retrospective</td>
<td>TEN 47 SJS 18</td>
<td>Methylprednisolone 1-1.5 mg/kg/day</td>
<td>27% / - 16.7% / -</td>
<td>16% more likely to die with steroids</td>
</tr>
</tbody>
</table>

IVIG

Proposed mechanism:

• Ability to block Fas and subsequent FasL-mediated apoptosis of keratinocytes

<table>
<thead>
<tr>
<th>Author &amp; year</th>
<th>Study type</th>
<th>Number patients</th>
<th>Treatment average total IVIG dose (g/kg)</th>
<th>Mortality with/without IVIG</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bachot et al. 2003⁹</td>
<td>Prospective open trial</td>
<td>34</td>
<td>1.0 (3 patients) 2.0 (31 patients)</td>
<td>32% / -</td>
<td></td>
</tr>
<tr>
<td>Metry et al. 2003¹⁰</td>
<td>Retrospective</td>
<td>7</td>
<td>2.0</td>
<td>0% / -</td>
<td>Early treatment correlated with longer time to response</td>
</tr>
<tr>
<td>Brown et al. 2004¹¹</td>
<td>Retrospective</td>
<td>45</td>
<td>1.6</td>
<td>41.7% / 28.6%</td>
<td></td>
</tr>
<tr>
<td>Yeung et al. 2005¹²</td>
<td>Prospective/retrospective controls</td>
<td>16</td>
<td>3.0</td>
<td>16.6% / 10%</td>
<td>Shorter time to cessation of progression and re-epithelialization with IVIG</td>
</tr>
<tr>
<td>Gravante et al. 2007¹³</td>
<td>Retrospective</td>
<td>32</td>
<td>2.0</td>
<td>41% / 27%</td>
<td></td>
</tr>
<tr>
<td>Stella et al. 2007¹⁴</td>
<td>Retrospective</td>
<td>31</td>
<td>2.8</td>
<td>26% / 75%</td>
<td></td>
</tr>
<tr>
<td>Yamane et al. 2007⁶</td>
<td>Retrospective</td>
<td>117</td>
<td>Max 1.2</td>
<td>9% / 3%</td>
<td></td>
</tr>
<tr>
<td>Schneck et al. 2008⁷</td>
<td>Retrospective</td>
<td>281</td>
<td>1.9</td>
<td>25.3% / 20.8%</td>
<td>No significant benefit from any treatment</td>
</tr>
<tr>
<td>Yang et al. 2009⁹</td>
<td>Retrospective</td>
<td>65</td>
<td>2.0</td>
<td>16.7% / 22.8%</td>
<td>Nonsignificant reductions in mortality, time of progression, and</td>
</tr>
</tbody>
</table>

The role of intravenous immunoglobulin in toxic epidermal necrolysis: a retrospective analysis of 64 patients managed in a specialized centre

Lee HY, Lim YL, Thirumoorthy T, and Pang SM.

British Journal of Dermatology. 2013
Study Design

• Primary Endpoint
  • Evaluate the risk of in-hospital mortality

• Study Methods
  • Single-center, retrospective analysis
  • 64 patients included from 2003 - 2010

## Enrollment

### Inclusion

- Diagnosed with SJS/TEN overlap or TEN
- Treated with IVIG

### Exclusion

- Exclusion Criteria
  - Diagnosed with SJS
  - No progression of disease
  - Primary treatment with corticosteroids

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Clinical Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>IVIG (n = 64)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex male, n (%)</td>
<td>26 (41)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>57 ± 19</td>
</tr>
<tr>
<td>Ethnicity, n (%)</td>
<td></td>
</tr>
<tr>
<td>Chinese</td>
<td>42 (66)</td>
</tr>
<tr>
<td>Malay</td>
<td>18 (28)</td>
</tr>
<tr>
<td>Indian</td>
<td>4 (6)</td>
</tr>
<tr>
<td>SCORTEN overall</td>
<td>2.6 ± 1.2</td>
</tr>
<tr>
<td>Cumulative dose IVIG (g/kg)</td>
<td>2.4 ± 0.8</td>
</tr>
<tr>
<td>Daily dosage (g/kg/day)</td>
<td>0.6 ± 0.2</td>
</tr>
<tr>
<td>Duration of administration (days)</td>
<td>4.0 ± 1.3</td>
</tr>
</tbody>
</table>

## Results

### Primary Predicted mortality, n | Observed mortality, n | Standardized mortality (95% CI)
--- | --- | ---
\(n = 64\) | 18 | 20 | 1.10 (0.62 – 1.58)

### Secondary Analyses

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Survivors (n = 44)</th>
<th>Non-survivors (n = 20)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>SCORTEN</td>
<td>2.2 ± 1.1</td>
<td>3.4 ± 1.0</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Low-dose IVIG &lt;3 g/kg (n = 42)</th>
<th>High-dose IVIG ≥ 3 g/kg (n = 19)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>SCORTEN</td>
<td>2.6 ± 1.2</td>
<td>2.2 ± 0.9</td>
<td></td>
</tr>
<tr>
<td>Observed mortality, n (%)</td>
<td>13 (31)</td>
<td>5 (26)</td>
<td>0.71</td>
</tr>
</tbody>
</table>

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Conclusions

• Limitations: retrospective design, varied dosing strategies

• Conclusions:
  • IVIG does not confer a significant survival benefit
Cyclosporine

Proposed mechanism:

• A calcineurin inhibitor with the ability to block the function of T cells
## Cyclosporine

<table>
<thead>
<tr>
<th>Author &amp; year</th>
<th>Study type</th>
<th>Number patients</th>
<th>Cyclosporine treatment</th>
<th>Mortality, n</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Valeyrrie-Allanore et al. 2010</td>
<td>Open phase II trial</td>
<td>29</td>
<td>3 mg/kg x 10 d, then 2 mg/kg x 10 d, then 1 mg/kg x 10 d</td>
<td>0</td>
<td>Progression and death rate lower than expected</td>
</tr>
<tr>
<td>Singh et al. 2013</td>
<td>Prospective open trial</td>
<td>11</td>
<td>3 mg/kg x 7 d, then 2 mg/kg x 7 d</td>
<td>0</td>
<td>May have encouraging role</td>
</tr>
<tr>
<td>Kirchof et al. 2014</td>
<td>Retrospective</td>
<td>64</td>
<td>3-5 mg/kg x 7 d</td>
<td>1</td>
<td>May have mortality benefit over IVIG</td>
</tr>
<tr>
<td>Lee et al. 2017</td>
<td>Retrospective</td>
<td>44</td>
<td>3 mg/kg x 10 d, then 2 mg/kg x 10 d, then 1 mg/kg x 10 d</td>
<td>3</td>
<td>Statistically insignificant survival benefit compared to supportive care</td>
</tr>
</tbody>
</table>

TNF-α Inhibitors

Proposed mechanism:

• Ability to inhibit granulysin and TNF-α secretion from blister cells
# TNF-α Inhibitors - Infliximab

<table>
<thead>
<tr>
<th>Author &amp; year</th>
<th>Study type</th>
<th>Number patients</th>
<th>Treatment</th>
<th>Mortality</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zarate-Correa <em>et al.</em> 2012</td>
<td>Case series</td>
<td>4</td>
<td>Single dose 300 mg infliximab on Day 1 or 2 after admission</td>
<td>0%</td>
<td>Disease progression halted in all 4 patients</td>
</tr>
<tr>
<td>Wojtkiewicz <em>et al.</em> 2008</td>
<td>Case report</td>
<td>1</td>
<td>Single dose 5 mg/kg infliximab after IVIG failure</td>
<td>0%</td>
<td>Within 24 hours of infliximab dose onset of new blisters stopped</td>
</tr>
<tr>
<td>Patmanidis <em>et al.</em> 2012</td>
<td>Case report</td>
<td>1</td>
<td>500 mg methylprednisolone IV bolus followed by 5 mg/kg infliximab IVIG 2g/kg x5 days</td>
<td>0%</td>
<td>Skin condition markedly stabilized by day 2 of admission</td>
</tr>
</tbody>
</table>


Randomized, controlled trial of TNF-α antagonist in CTL-mediated severe cutaneous adverse reactions

Objectives

• Primary endpoint:
  • Time required to heal skin erosions and oral mucosa and to begin re-epithelialization

• Secondary monitoring parameters:
  • Adverse events
  • Mortality rates

Study Methods

• Single-center, prospective, open-label, randomized controlled unblinded trial

• Randomized 1:1
  - 25 mg (or 50 mg if >65 kg) etanercept SQ injection twice a week
  - 1-1.5 mg/kg/day prednisolone IV
  - Treated until skin lesions healed

• 96 patients randomized, 71 completed to efficacy analysis

## Enrollment

### Inclusion
- Older than 4 years
- Diagnosed with probably/definite SJS/TEN

### Exclusion
- Pregnant or breastfeeding
- Allergy to any TNF-α inhibitor
- Active/latent tuberculosis
- Severe, active infection and septicemia
- Carriers of active hepatitis B or C
- Suspected carriers of HIV with CD4 Tcell count <200
- Poor compliance or safety concerns

## Baseline Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>All n = 91</th>
<th>Etanercept n = 48</th>
<th>Corticosteroid n = 43</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>56.09 ± 20.81</td>
<td>52.73 ± 16.78</td>
<td>59.84 ± 24.20</td>
<td>0.112</td>
</tr>
<tr>
<td>Sex, n (%)</td>
<td></td>
<td></td>
<td></td>
<td>0.658</td>
</tr>
<tr>
<td>Male</td>
<td>40 (44)</td>
<td>20 (41.7)</td>
<td>20 (46.5)</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>51 (56)</td>
<td>28 (58.3)</td>
<td>23 (53.5)</td>
<td></td>
</tr>
<tr>
<td>Skin detachment, n (%)</td>
<td></td>
<td></td>
<td></td>
<td>0.858</td>
</tr>
<tr>
<td>BSA ≥ 10%, n (%)</td>
<td>35 (38.5)</td>
<td>18 (37.5)</td>
<td>17 (39.5)</td>
<td></td>
</tr>
<tr>
<td>BSA &lt;10%, n (%)</td>
<td>56 (61.5)</td>
<td>30 (62.5)</td>
<td>26 (60.5)</td>
<td></td>
</tr>
<tr>
<td>SCORTEN mean</td>
<td>1.85 ± 1.29</td>
<td>1.95 ± 1.36</td>
<td></td>
<td>0.722</td>
</tr>
</tbody>
</table>

# Results

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Etanercept n = 38</th>
<th>Corticosteroid n = 33</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median time for skin healing, d</td>
<td>14</td>
<td>19</td>
<td>0.010</td>
</tr>
<tr>
<td>Predicted mortality, %, mean</td>
<td>$17.7 \pm 20.5$</td>
<td>$20.3 \pm 25$</td>
<td>0.722</td>
</tr>
<tr>
<td>Observed mortality, n (%)</td>
<td>4 (8.3)</td>
<td>7 (16.3)</td>
<td>0.266</td>
</tr>
<tr>
<td>GI hemorrhage, %</td>
<td>2.6</td>
<td>18.2</td>
<td>0.03</td>
</tr>
<tr>
<td>Serious adverse events, n</td>
<td>5</td>
<td>9</td>
<td>-</td>
</tr>
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Conclusion

• Strengths: randomized controlled trial
• Limitations: unblinded

• Conclusion:
  • Etanercept reduced predicted mortality, rates of GI hemorrhage, and time to skin healing in moderate-to-severe SJS/TEN compared to corticosteroids
  • Further studies in combination with other treatment strategies needed
Summary of Adjuvant Therapies

**Steroids**
- Have been associated with increased infection rates, duration of stay, and mortality
- Possible beneficial role with short-term therapy or as addition to other therapies

**IVIG**
- Conflicting evidence
- Most recent studies show no survival benefit over supportive care

**Cyclosporine**
- Most recent study shows no survival benefit over supportive care
- More research required

**TNF-α inhibitors**
- Best evidence for mortality benefit
- Further research required to determine ideal treatment regimen
Plasmapheresis

Proposed mechanism:

- Can enhance the removal of medications and activated immune cells from plasma

- Studies have not consistently shown benefit

- May be considered if other treatments are failing


Thalidomide

• Use is contraindicated in SJS/TEN

• Double-blind, randomized placebo-controlled trial (n =12)
  • Mortality increased in thalidomide group vs placebo (83% vs 30%)
  • Trial was discontinued early

Optimal treatment of SJS/TEN includes supportive care and extended duration corticosteroids.

a) True
b) False
Optimal treatment of SJS/TEN includes supportive care and extended duration corticosteroids.

a) True

b) False
Summary

• SJS/TEN characterized by full-thickness epidermal necrosis and keratinocyte apoptosis

• Medications are the most common cause of SJS/TEN

• There is no gold-standard of treatment
  • Stop offending agent
  • Supportive care
Discussion & Questions
Study References