Airway involvement and mechanical ventilation in Steven Johnson Syndrome and Toxic Epidermal Necrolysis management

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ABSTRACT

Steven-Johnson syndrome (SJS) and Toxic Epidermal Necrolysis (TEN) are severe drug allergic reactions characterized by skin and mucosal membrane detachments. Most of the literature focuses only on the skin and ocular mucosal damage, but more severe and life-threatening mucosal damage may actually occur in the respiratory tract. This airway involvement may cause an acute complication, e.g. acute respiratory failure, and chronic complications, e.g. bronchiolitis organizing pneumonia, bronchiectasis, and restrictive bronchiolitis. The presence of airway involvement in SJS/TEN requires a more detailed examination, ranging from examination of the ear, nose, and throat (ENT), to fiberoptic bronchoscopy done by a skilled clinician to determine the presence of bronchial epithelial detachment. A higher percentage of skin and mucosal detachment is associated with a greater need for mechanical ventilation. Male sex, age, low serum bicarbonate, high serum urea, and higher amount of infiltrate on chest X-rays are also associated with a higher risk for mechanical ventilation in patients with SJS/TEN. The general indications for intubation and mechanical ventilation in patients with SJS/TEN are respiratory failures, inability to clear the airway, shock, neurologic disorder, and uncontrollable pain. More specific indications for intubation and mechanical ventilation are oral involvement with an initial total body surface area (TBSA) during hospital admission was ≥70%, or progression of TBSA ≥15% in the first 3 days of hospitalization, or neurological failure as well, requiring a breathing apparatus to maintain the airway. Airway obstruction can cause respiratory failure as well, requiring a breathing apparatus to maintain the airway. To date, there are no clear guidelines and little literature on the need for mechanical ventilation in patients with SJS/TEN. We aim to review the role and use of mechanical ventilation in the management of SJS/TEN.

Airway Involvement in SJS/TEN

Airway involvement may occur as an acute complication or chronic complication of SJS/TEN. The prevalence of airway involvement for SJS and TEN was 3.8% and 8.6%, respectively. Almost 90% of airway involvement in SJS/TEN cases was occurred in the oral cavity, lips, buccal mucosa, and gum.7 However, in some cases, SJS/TEN may result in some life-threatening pulmonary complications. Some studies have reported some serious airway obstruction and pulmonary complications of SJS/TEN.8–15 The airway involvement in SJS/TEN may manifest as an acute complication during hospitalization or as a chronic pulmonary sequela due to decreased pulmonary function.9 Acute pulmonary complication includes pneumonia, pneumothorax, mediastinal emphysema, bronchitis, and bronchiolitis obliterans. Pneumonia may occur in 30% of acute respiratory complications of SJS/TEN and is associated with Mycoplasma

INTRODUCTION

Steven-Johnson Syndrome (SJS) and Toxic Epidermal Necrolysis (TEN) are severe and life-threatening allergic reactions.3,4 This syndrome is usually caused by drugs or their metabolites, such as carbamazepine, quinolones, and sulfonamides.5 This is a rare disease with an incidence of 1-2 per 1 million people per year. The mortality rate for SJS/TEN is considered high, which is about 3%-4% for SJS and 30%-50% for TEN.4

In SJS/TEN, there is skin and mucous membranes damage due to the apoptosis of keratinocytes.4,5 SJS and TEN are distinguished by the surface area of the body undergoing tissue necrosis due to an allergic reaction. In SJS the affected body surface area is less than 10%, if the affected body surface area is more than 30% it is called TEN, and the affected surface area is 10%-30% is called SJS/TEN overlap.4 Damage to skin and mucosal tissue does not only occur on the face and trunk, but can also occur in the digestive, respiratory, and ocular mucosa.5

Although mucosal damage to the respiratory tract is rare, it can lead to edema of the larynx and hypersecretion of secretions resulting in airway obstruction. Airway obstruction can cause respiratory failure as well, requiring a breathing apparatus to maintain the airway. To date, there are no clear guidelines and little literature on the need for mechanical ventilation in patients with SJS/TEN. We aim to review the role and use of mechanical ventilation in the management of SJS/TEN.
A retrospective cohort study showed that 25% of SJS/TEN cases with airway involvement required mechanical ventilation due to acute respiratory failure. Bronchial epithelial lesions were found in 40% of them. These patients with specific bronchial epithelial lesions experienced progressive respiratory symptoms within 48 hours of hospital admission. A similar result was reported by Lebargy et al. where 27% of SJS/TEN cases had bronchial epithelial lesions. Most common radiologic findings in acute pulmonary complications associated with SJS/TEN are lung infiltrates, pleural effusions, and pneumothorax.

Chronic pulmonary sequelae are more common in TEN than in SJS. Some chronic pulmonary complications of SJS/TEN are bronchiolitis organizing pneumonia (BOOP), bronchiectasis, constrictive bronchiolitis, and bronchiolitis obliterans. The onset of chronic pulmonary sequelae is varied. Some cases may have these complications as early as a week after TEN/SJS, while others may have these complications after a month.

**Risk Factor of Airway Involvement and Mechanical Ventilation in SJS/TEN**

There are several studies specifically examining factors associated with the need for mechanical ventilation in patients with SJS/TEN. These factors may be useful for predicting which patients may experience worsening so that intubation and mechanical ventilation can be done earlier. Beck et al stated in their study that there are several modifiable and non-modifiable factors related to the need for mechanical ventilation in SJS/TEN patients. Male sex was significantly associated with the need for mechanical ventilation and a higher risk of mortality ($p = 0.043$). However, age and race did not have a significant relationship with the need for mechanical ventilation. Other factors that were significant risk factors for mechanical ventilation in SJS/TEN patients was the number of infiltrates on chest X-ray upon admission, development of acute kidney injury within 72 hours of admission, and low serum bicarbonate (< 20 mM/L) within 72 hours of admission ($p = 0.012$). Another study was done by de Prost et al. also found some risk factors that were significantly associated with the need for mechanical ventilation in patients with SJS/TEN, including low serum bicarbonate (< 20 mM/L), high serum urea (>10 mM/L), TBSA 10%-30% upon admission, leukocytosis (>12,000/mm³), severe anemia (Hb < 8 g/dL), and extensive pulmonary infiltrates. A meta-analysis study also showed that bacteremia/sepsis, shock, multiple organ failure, and higher TBSA involved were significant risk factors for mechanical ventilation in patients with SJS/TEN. Another similar result was obtained by Williams et al. in their case-control study. Williams et al. found that oral involvement, initial TBSA >70%, and progressive TBSA (>15%) during admission were significant risk factors for mechanical ventilation in patients with SJS/TEN.

De Prost et al. found that SCORTEN is associated with a greater need for mechanical ventilation. SCORTEN is a specific score used to assess the severity of SJS/TEN cases. SCORTEN has high accuracy in predicting mortality in SJS/TEN patients. This scoring system consists of seven indicators (Table 1). However, Williams et al. in their study did not find that SCORTEN as the significant risk factor for the need for mechanical ventilation in patients with SJS/TEN. They did not find any difference in SCORTEN score between the patient who needs intubation/mechanical ventilation and the patient who did not need intubation/mechanical ventilation ($p = 0.20$).

Therefore, the association between SCORTEN to the need for mechanical ventilation remains controversial.

### Classification of Airway Involvement in SJS/TEN

The U.K guidelines classify SJS/TEN patients with airway involvement into three groups. This classification is based on the respiratory symptoms, hypoxemia, and the onset of the development of hypoxemia. Group 1 is patients without hypoxemia during the acute phase of SJS/TEN. This group usually has no chronic pulmonary sequelae and very low mortality. Group 2 is patients with early respiratory symptoms, such as dyspnea and tachypnea, and has normal radiologic imaging on admission, but later develops diffuse pulmonary infiltrates. This group usually needs mechanical ventilation and has a higher mortality rate which is 70%. Group 3 is patients with delayed respiratory symptoms. These delayed respiratory symptoms include pleural effusion, pneumonia, and atelectasis. There is no epithelial detachment found in these patients and these patients usually did not need mechanical ventilation. However, this group also has a poor prognosis due to chronic pulmonary sequelae and also has a high mortality rate (40%).

### Management of Airway Involvement in SJS/TEN

A study by Bhullar et al. found that most patients with SJS/TEN were intubated for operative management and dressing change. Dressing change may cause significant pain in patients with TEN due to a higher TBSA than SJS. Only

### Table 1. SCORTEN score

<table>
<thead>
<tr>
<th>Prognostic Factors</th>
<th>Score</th>
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<tbody>
<tr>
<td>Age (&gt;40 years old)</td>
<td>1</td>
</tr>
<tr>
<td>Tachycardia (&gt;120 beats/minute)</td>
<td>1</td>
</tr>
<tr>
<td>Neoplasia</td>
<td>1</td>
</tr>
<tr>
<td>Initial detachment (TBSA &gt;10%)</td>
<td>1</td>
</tr>
<tr>
<td>High serum urea (&gt;10 mmol/L)</td>
<td>1</td>
</tr>
<tr>
<td>High serum bicarbonate (&lt;20 mmol/L)</td>
<td>1</td>
</tr>
<tr>
<td>Blood glucose (&gt;14 mmol/L)</td>
<td>1</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Interpretation</th>
<th>Mortality Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-1</td>
<td>3%</td>
</tr>
<tr>
<td>2</td>
<td>13%</td>
</tr>
<tr>
<td>3</td>
<td>35%</td>
</tr>
<tr>
<td>4</td>
<td>58%</td>
</tr>
<tr>
<td>≥5</td>
<td>90%</td>
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Abbreviations:
- TBSA: Total body surface area
23.6% of patients in their study were intubated due to complications of the airway involvement. However, de Prost et al. found in their study that 78% of their patients were intubated due to acute respiratory failure.

When airway involvement is suspected in patients with SJS/TEN, a careful examination of the ear, nose, and throat must be done as the initial assessment. A pulmonary function test, arterial blood gases, and thorax computed tomography scanning or chest x-ray should be obtained upon admission. If the patients had severe respiratory symptoms and hypoxemia, they should be closely monitored and immediately transferred to the burn unit or intensive care unit when available. Patients with severe airway involvement, especially dysphonia or dyspnea, may be evaluated using nasal fiberoptic bronchoscopy. The nasal fiberoptic bronchoscopy examination must be done by a skilled clinician to avoid further mucosal injury. Through this invasive examination, the clinician may identify bronchial epithelial detachment due to bronchial necrosis. This examination also determines the best possible intubation route for the patient. When this invasive diagnostic tool is not possible, the clinician may use a clinical indicator or early predictive factors to determine the need for mechanical ventilation in a patient with SJS/TEN. It should be noted that a normal chest x-ray did not exclude bronchial epithelial lesions. Since a higher percentage of TBSA involved is associated with a higher need for mechanical ventilation, early identification and immediate withdrawal of causative agents will help to prevent further airway obstruction or progression of bronchial epithelial lesions in this patient.

The general clinical indication of intubation and mechanical ventilation in patients with SJS/TEN is respiratory failure, inability to clear the airway, shock, decreased consciousness, and pain control. Seminario-Vidal et al. and Williams et al. proposed specific indications of mechanical ventilation in SJS/TEN which is oral involvement with one of the following: (1) initial TBSA during hospital admission was ≥70%; (2) increase in TBSA ≥15% in the first 3 days of hospitalization; (3) neurological disorders, including loss of consciousness and stroke, which causes the patient to be unable to maintain a patent airway; (4) documented airway involvement based on direct laryngoscopy examination. However, these criteria are not yet validated and still need further studies.

**CONCLUSION**

Airway involvement was uncommon yet life-threatening in patients with SJS/TEN. Some patients even require intubation and mechanical ventilation due to respiratory failure. Patients with severe respiratory symptoms and hypoxemia also have a poorer prognosis due to chronic pulmonary sequelae and a higher mortality rate. Therefore, the clinician should perform a complete and detailed examination of SJS/TEN patients with suspected airway involvement, especially the nasal fiberoptic bronchoscopy. If this invasive examination is not possible, the clinician can use other clinical indicators to determine the use of mechanical ventilation in SJS/TEN patients with airway involvement.

**CONFLICT OF INTEREST**

The author reports no conflicts of interest in this work.

**FUNDING**

This study did not involve third party sponsor or funding source.

**AUTHOR CONTRIBUTION**

All authors contribute equally in all phases of the study.

**REFERENCES**


