

# Anesthetic management and outcomes of patients with Steven-Johnson Syndrome—A retrospective review study

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## Abstract

**Background and Aims:** Steven-Johnson Syndrome (SJS) is a rare and severe form of erythema exudative multiforme. Multisystem involvement in SJS and the suspicion of precipitation of the disease with exposure to anesthetic drugs makes anesthesia a challenging task. The concerns during anesthesia are the mucosal lesions and special care that is required to prevent injury to the oropharynx and larynx during airway management and also the drugs used for anesthesia. In the literature, very few isolated case reports or case series are available. Here, we have analyzed the cases of SJS coming for ophthalmic anesthesia, taking into consideration factors like mode of presentation, precipitating factors, associated diseases, types of anesthesia, anesthetic modifications, and various drugs used during anesthesia.

**Material and Methods:** The electronic medical records of 497 cases of SJS who required interventions like ophthalmic examination or surgery (either under local or general anesthesia) over a period of 18 months were analyzed retrospectively. The records were reviewed to obtain the concerned details like anesthesia-inducing agents, muscle relaxants, inhalational agents, and analgesics. The problems concerned with monitoring and intubation were also noted. The data were analyzed and presented as frequency and percentage.

**Results:** Patient age ranged between 9 months and 72 years. Many surgeries were conducted under general anesthesia (441) although a few required local (peribulbar block) anesthesia (56). The drugs administered for general anesthesia were sevoflurane, isoflurane, propofol, thiopentone, vecuronium, and atracurium and those administered for pain management were fentanyl, tramadol, butorphanol, and paracetamol. The patients who were sensitive to nonsteroidal anti-inflammatory drugs (NSAIDs) and paracetamol were not administered the same. None of the patients reacted adversely to the different drugs used for anesthesia.

**Conclusion:** Identifying the precipitating factors, understanding the pathophysiology and its implications for anesthesia will help in successfully managing anesthesia in the rare cases of SJS.

**Keywords:** Airway problems, drugs and sensitivity, general anesthesia, ophthalmic surgery, sequel of SJS, Steven-Johnson Syndrome (SJS)

## Introduction

Steven-Johnson Syndrome (SJS) was first described by two pediatricians (A M Stevens and FC Johnson) in 1922 in

New York City. The syndrome was noticed in two children and was precipitated by infection.<sup>[1]</sup> SJS is a rare, uncommon, and acute exfoliating disease of the skin and mucous membrane<sup>[2]</sup> with an incidence rate of 1–7 per million,<sup>[3]</sup> and the mortality rate of 3–34%.<sup>[4]</sup> SJS is considered a delayed-type

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hypersensitivity reaction with variable severity. In the initial stages, manifestations include sore throat, malaise, fever, erosions, small blisters, dusky, purpuric maculae, or atypical target lesions.<sup>[5,6]</sup> The involvement of mucous membranes is seen in approximately 90% of the affected patients.<sup>[7]</sup> This can lead to short-term dysfunction, morbidity, and long-term complications with fibrosis and strictures. The sequelae of SJS are due to mucosal ulceration followed by scarring and stricture, resulting in significant deterioration of the function of the affected organ systems.<sup>[3]</sup> The most commonly affected organ is the eye after the skin and is reported in 75% of cases ranging from mild conjunctivitis to panophthalmitis with corneal destruction.<sup>[8]</sup>

Due to the availability of improved medical facilities and management, there is an early recognition of cases of SJS making survival easy. This has resulted in more of the ophthalmic sequel patients accessing management of the same. These patients require anesthesia for various ophthalmic procedures of varying duration. For the safe conduct of anesthesia, it is imperative for the anesthesiologist to understand the pathophysiology, the precipitating factors, the management modalities, and the anesthetic considerations. In the literature, only a few isolated case reports and series are available. However, we have an electronic record of a large number of cases with SJS. Hence, we have undertaken the study of observing anesthetic implications in SJS patients who are undergoing anesthesia for ophthalmic procedures.

## Material and Methods

The patients of SJS and those with the sequel of SJS who come to our institution from all over the world for ocular examination and ophthalmic surgical procedures under anesthesia were included in the study. After obtaining approval from the ethics committee, a retrospective analysis was done reviewing the electronic medical records between January 2016 and June 2017. The patient medical records were reviewed to obtain the following: demographic features, medical and medication history, known drug allergies or any other causes for precipitation of the syndrome, the extent of skin and mucous membrane involvement, and airway problems. On the day of surgery, in the operating room, the various drugs used for anesthesia, anesthetic management, and any untoward reaction to the anesthetic drugs were noted.

## Results

A total number of 497 cases of SJS had undergone surgical procedures under anesthesia between January 2016 and June 2017. Among them, 57.14% (284) cases were new patients

and the rest were repeat cases. The patients' age ranged between 9 months and 72 years, with the majority of patients being above the age of 20 years [Table 1]. Various coexisting diseases in these patients are shown in Table 2. Epilepsy was the most common disorder followed by diabetes, hypertension, chronic renal failure, and hypothyroidism.

Drug allergy was identified as a precipitating factor in 389 (78.3%) cases and no such factors were seen in 108 (21.7%) cases. Commonly identified drugs as causative agents were a combination of sulphonamides, phenytoin, and NSAIDs. The other isolated drugs causing precipitation were sulphonamides, phenytoin, aspirin, paracetamol, chemotherapy, and Vitamin B-complex. The drugs like ciprofloxacin, cefotaxime, gentamycin, amoxicillin, tetracycline, and  $\beta$ -lactamases were the antibiotics responsible for precipitating SJS [Table 3].

Table 4 shows patients with SJS who were on various medications for symptomatic relief and for the coexisting diseases. The majority of the cases were on prednisolone eye drops and few of them on oral prednisolone therapy. Other drugs received by these patients included bronchodilators, phenytoin, antihypertensives, etc., [Table 4].

General anesthesia was required in 88.7% (441) cases and local anesthesia in 11.3% (56) cases [Table 5]. Endotracheal intubation and controlled ventilation were required for 72.4% patients whereas some cases were managed with laryngeal mask airway (LMA) and spontaneous ventilation.

**Table 1: Demographic data**

	Number of cases	Percentage of cases
Age in yrs		
9/12-10	47	9.45%
11-20	111	22.33%
>20	339	68.21%
Sex distribution		
Male	269	54.12%
Female	228	45.88%

**Table 2: Associated disorders**

Associated disorders	Number of cases	Percentage of cases
Epilepsy	23	4.62%
Diabetes	19	3.82%
Hypertension	9	1.81%
CRF on Haemodialysis	2	0.40%
Hypothyroidism on R <sub>x</sub>	2	0.40%
Koch's on R <sub>x</sub>	1	0.20%
Dog bite	1	0.20%
Gout	1	0.20%
Retroviral sero-positive	2	0.40%

Anesthetic induction agents used were sevoflurane (58.7%), propofol (35.6%), and thiopentone (5.6%). Vecuronium (76%) and atracurium (24%) were the muscle relaxants used. The other drugs used were fentanyl, tramadol, butorphanol, and dexmedetomidine [Table 6]. Some patients required multiple surgeries and repeated exposure to general anesthesia [Table 7].

## Discussion

SJS may be precipitated by single or multiple etiological factors.<sup>[3]</sup> The main four etiological factors responsible for SJS are infections, drug-induced, malignancy-related, and idiopathic. Our study results showed that 78.5% of cases were due to drugs or infections (medication to infection) as a triggering agent. The combination of sulphonamides, phenytoin, and NSAIDs was responsible for precipitating the syndrome in 69.82% of the cases.

The initial lesions of SJS are diffuse erythematous macules with purpuric, necrotic centers and overlying blisters that may progress to skin slough, resulting in widespread superficial ulcers and loss of the epidermal barrier.<sup>[3]</sup> Fluid and protein loss from the weeping epithelium can lead to fluid and electrolyte imbalance with hypoproteinemia. Anesthetic concerns here include maintenance of skin and mucous membrane integrity, safe airway management, and prevention of heat and fluid loss. Difficulties may arise with getting venous access, application of monitors and even with anesthesia face mask, airways, laryngoscopy, and intubation.<sup>[2]</sup>

Long-term sequelae like dry eye, synechia, corneal ulceration, perforation, and permanent sclerotic changes<sup>[8,9]</sup> are common in these patients. These patients need anesthesia for various procedures. Our patients were posted for examination under anesthesia (43), for tarsorrhaphy (32), for amniotic membrane graft (63), for mucous membrane graft (321), for penetrating keratoplasty (PKP), Boston keratoprosthesis (51), and keratolimbic allografting (37).

The challenge in administering anesthesia depends on the severity and the duration of the disease. Handling and transfer of the patients were kept to a minimum to prevent further epithelial damage or rupture of the bullae. In view of the patients' immune-compromised state and susceptibility to infection (especially respiratory),<sup>[10-12]</sup> strict aseptic precautions were taken in the perioperative period at all stages. Monitoring of patients was difficult in some; as standard probes and electrodes were self-adhesive. In 17 patients, ECG electrodes could not be placed due to the lesions on the body which were in the acute stages of the disease so intradermal needle

**Table 3: Precipitating Drugs**

Precipitating drugs	Number of cases	Percentage of cases
Combination of sulphonamides, phenytoin and NSAIDS	347	69.82
Isolated drugs		
Sulphonamides	20	4.03%
Phenytoin	10	2.03%
Paracetamol	2	0.40%
Chemotherapy	1	0.20%
Vitamin B-complex	1	0.20%
Antibiotics		
Ciprofloxacin	2	0.40%
Cefotaxime	1	0.20%
Amoxicillin	2	0.40%
Tetracycline	1	0.20%
β lactamases	2	0.40%

NSAIDs: Nonsteroidal anti-inflammatory drugs

**Table 4: Medication History**

Various drugs	Number of patients	Percentage of cases
Oral prednisolone	11	2.21%
Prednisolone eye drops	259	52.11%
Valproate	3	0.62%
Levetiracetam	4	0.80%
Antihypertensives	11	2.21%
Bronchodilators	54	10.86
OHA	3	0.60%
Insulin	1	0.20%
Tramadol	15	3.02%
Clopidogrel/Ecosprin	11	2.21%
Cyclosporine	13	2.62%
Gabapentin	1	0.20%

**Table 5: Type of anesthesia**

Type of anesthesia	Number of cases	Percentage of cases
Local Anesthesia	56	11.3%
Lignocaine	56	Local anaesthetics were used in combination.
Bupivacaine	56	
Ropivacaine	54	
General anesthesia	441	88.7%
Spontaneous ventilation	56	12.7%
Controlled ventilation	385	87.3%
LMA	79	11.2%
ET intubation	362	72.8%

LMA: Laryngeal mask airway; ET: Endotracheal

electrodes were used. Cardiac involvement in the form of myocarditis, atrial fibrillation, or pericarditis necessitates the ECG tracings.<sup>[10]</sup> Padding or polyvinyl chloride (PVC) film was used beneath the noninvasive blood pressure (NIBP) cuff to reduce the shearing forces on the arm. A similar modification was used in other studies.<sup>[13]</sup> Invasive blood pressure monitoring is justified for longer procedures and major surgeries.<sup>[14]</sup> This was not required in our cases. Clip-on

**Table 6: Anesthetic Agents used**

Anesthetic agents	Number of cases	Percentage of cases
Induction drugs		
Sevoflurane	259	58.7%
Propofol	157	35.6%
Thiopentone	25	5.6%
Muscle relaxants		
Vecuronium	335	76%
Atracurium	106	24%
Inhalational anesthetics		
Sevoflurane	284	64.5%
Isoflurane	148	33.5%
Halothane	9	2%
Analgesics		
Fentanyl	239	54.2%
Tramadol	78	17.7%
Butorphanol	123	27.9%
Dexmedetomidine	67	15.2%

**Table 7: Frequency of Anesthetic exposure**

Number of times exposure	Number of patients exposed	Percentage of cases
1	174	35.01%
2	61	12.27%
3	23	4.63%
4	12	2.41%
5	6	1.21%
6	4	0.80%
7	2	0.40%
8	2	0.40%

probes were used to monitor oxygen saturation. Temperature monitoring was done by skin probes with lubrication as these patients are prone to hypothermia.

Creaseless sheets and foam/gel padding was used to protect the patients' heels and elbows from shearing effects. Lesions of the oral, laryngeal, and tracheal mucosa may cause difficulty in maintaining the airway. Even the application of the anesthetic facemask can abrade and denude the involved facial epithelium. The use of airways may cause bleeding and push the tissue debris into the pharynx and larynx.<sup>[10]</sup> One size smaller than the standard-sized endotracheal tube was used to secure the airway and the cuff was inflated gently maintaining low pressure. All our patients were intubated with right angle endotracheal (RAE) tubes for ophthalmic surgeries. Endotracheal intubation with controlled ventilation was used in 72.4% of cases. We did not encounter any difficulty in intubation in our cases. An intubation rate of 48% of 25 patients undergoing 121 procedures has been reported.<sup>[15]</sup> In another study, 64 patients were intubated by direct laryngoscopy without difficulty and three patients were intubated with fiberoptic tracheal intubation due to contracture in the neck and limited mouth opening.<sup>[13]</sup>

Coexisting disease and many medications that are used for the symptomatic relief can have anesthetic implications and may require modifying the drugs used for anesthesia. Induction of general anesthesia with ketamine or etomidate could provide better hemodynamic stability when compared to thiopentone or propofol.<sup>[11]</sup> Propofol, thiopentone, and ketamine were used as intravenous anesthetic agents in some other series.<sup>[15-17]</sup> In our study, propofol (35.6%) and thiopentone (5.6%) were used for intravenous induction. In other studies, ketamine was used as the sole anesthetic agent for small surgical procedures.<sup>[15,16,18-19]</sup> Propofol may cause precipitous fall in blood pressure in hypovolemic patients if not used in titrated doses. Ketamine has the added advantages of analgesic effect, preservation of the protective airway reflexes and maintenance of spontaneous respiration. Etomidate was used by Kwass and Chow<sup>[11]</sup> in one case report.

Inhalational induction with sevoflurane was safely used in pediatric patients with a titrated concentration in 58.7% of patients in our study. Other published reports have mentioned inhalational induction in 21–73.4% cases.<sup>[15,16]</sup> LMA with spontaneous breathing was used here in 27.4% of cases for short procedures. The LMA can be a useful adjuvant in the management of difficult airways and also for the management of short surgical procedures. One size smaller than the standard size should be used.<sup>[13]</sup>

Non-depolarizing muscle relaxants may have slightly prolonged the duration of action secondary to change in volume of distribution as a result of hypoalbuminemia<sup>[10]</sup> or hypovolemia.<sup>[13]</sup> However, vecuronium (76%) and atracurium (24%) were used with no prolongation of the duration of action in our patients. Several other studies have also mentioned the use of atracurium and vecuronium safely without encountering difficulties.<sup>[15-16,20]</sup> Rocuronium was used in one case series<sup>[11]</sup> with no change in the pattern of drug action.

Short-acting narcotics fentanyl was used in titrated doses to prevent respiratory depression in our study. Fentanyl was also used as an analgesic in another case series.<sup>[11]</sup> NSAIDs were avoided in patients with a history of sensitivity to the drug. Tramadol, butorphanol, and dexmedetomidine were used safely. Kwass and Chow<sup>[11]</sup> reported the use of dexmedetomidine infusion and sevoflurane for maintenance of anesthesia in one patient and sevoflurane and fentanyl in another.

In our study, anesthesia was maintained with oxygen, nitrous oxide, and inhalational anesthetic with intermittent positive pressure ventilation in 72.4% cases. Eleven (2.21%) patients received stress dose corticosteroids on the day of surgery as

they were on long-term steroid therapy to prevent sequelae. Corticosteroids, either topical or systemic, have been used in the management of SJS.<sup>[21,22]</sup>

Regional anesthesia has been found to be safe in SJS patients. There are reports of surgery done under regional anesthesia alone, such as cesarean section under spinal anesthesia.<sup>[23]</sup> Splenectomy and cholecystectomy performed under general anesthesia and continued epidural blockade have also been described.<sup>[24]</sup> In our study, peribulbar block was given in 56 (11.4%) cases using lignocaine, bupivacaine, and ropivacaine without any adverse events. Thus, all the anesthetic agents (local and general) used in our study were observed to be safe without encountering any adverse effects.

## Summary

SJS is a rare disorder that involves the skin and mucous membrane. Understanding the pathophysiology and the course of the disease will help in the successful management of anesthesia. Proper preoperative evaluation, identification of the precipitating agents in order to avoid them, a continuation of preoperative medications, and other immunosuppressants or steroids is essential. Extreme care should be taken while transferring the patients when the lesions are fresh. The patients with involvement of the respiratory tract and pleura demand special attention including the application of face mask, laryngoscopy, intubation, and suction with extra lubrication when general anesthesia is chosen. Our study concludes that anesthetic drugs can be safely used in SJS patients.

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## Conflicts of interest

There are no conflicts of interest.

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