Authors' reply

We thank Dr. Pasricha for his interest in our paper and his comments about the use of steroids in Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN). It is apparent from the title that our paper was focused mainly on the etiological agents and outcome of SJS and TEN.[1] The role of steroids in the treatment of SJS-TEN generates a lot of discussion and the recommendation has recently been published in the IADVL therapeutic guidelines.[2] In our report we have used systemic steroids in all except one.[1]

Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are severe adverse cutaneous drug reactions characterized by massive keratinocyte apoptosis. It has been shown that the apoptosis is mediated by the drug specific cytotoxic T cells through the activation of the Fas receptor by increased Fas ligand expression, via the perforin / granzyme pathway. Several cytokines produced by the T cells, macrophages,and keratinocytes, upregulate the adhesion molecules and enhance the expression of Fas and FasL on keratinocytes.[3,4] Hence there are enough reasons to start immunosuppressive therapy such as steroids in the early evolving stage of the disease. The exact mode of action of steroids in SJS/TEN is not known. But they have a plethora of immunomodulating / immunosuppressive and anti-apoptotic effects which will hamper the events leading to apoptosis.

There are many reports of better outcomes with the use of steroids in SJS/TEN.[5,6] In a report of 52 cases of SJS and 65 cases (2000-2006) of TEN from Japan, the authors have used methyl prednisolone pulse (125-1000 mg/day) for 3 days. They have concluded that the mortality rates for patients with SJS and TEN were 1.9% and 6.2% respectively which has decreased from 21.6% (58/269) during previous 17 years (1981-1997) in which period steroids were rarely used.[7] Tripathi *et al* in their report of 67 cases with SJS, 66 cases recovered with steroid therapy.[8] In a recent report of 12 cases of SJS/TEN, from Netherlands, the authors have used dexamethasone pulse therapy, 11 patients recovered and only one died due to brain metastasis while his skin had healed.[9]

There are some conflicting views on steroid usage in SJS/TEN. It is reported that systemic corticosteroids can prolong wound healing, increase the risk of infection, mask early signs of sepsis, and may precipitate gastrointestinal bleeding, thus increasing mortality.[3] What we believe from our experience is that use of steroids in a fully developed case of SJS/TEN or prolonged use of steroids, might be detrimental and predispose to sepsis and other complications.

The fatality in SJS/TEN is largely caused by sepsis, thrombocytopenia, leucopenia, electrolyte imbalance, total body surface area involvement, renal involvement, and delay in referral to special burns centre. TEN itself predisposes to sepsis due to loss of skin barrier, hospitalization and nosocomial infection and use of empirical antibiotics. Sepsis is one of the most important causes of death in TEN (Odds Ratio 304).[10] The mortality rate varies from 20-60%.[10] In a retrospective review of 56 patients with TEN over a period of 13 years, the mortality was 35.7%, which was not associated with steroid use.[10] Most of the deaths occur in patients with TEN as is evident in our study.[1] The proportion of SJS, TEN and SJS-TEN overlap in different series contributes to varied mortality rates.

Intravenous immune globulin (IVIG) is also found to be useful in SJS/TEN.[11-15] It interferes with Fas-FasL interactions. The recommended dose is 1g/kg/day for 3 days. In a multicenter retrospective study involving 14 European and American centers, IVIG was used in 48 TEN patients and the survival rate was 88%.[11] However some data show no benefit on mortality or progression.[16,17] In one of the recent report by Faye and Roujeau, nine different series published in indexed journals were analyzed. Among the 156 patients of SJS or TEN treated with IVIG, 32 patients died. When the analysis was restricted to 5 series that included some comparison with the expected deaths, the mortality was 27% versus an expected rate of 30%.[18] This clearly shows that the use of IVIG in SJS/TEN is questionable. The additional limiting factor of IVIG is the high cost.

Overall from our personal experience and also from the literature search, it seems that steroids or other immunosuppressive drugs have definite role in SJS/TEN.

We agree with Dr. Pasricha that 1) Steroids should be used in SJS/TEN as immune mechanisms are involved in the massive keratinocyte necrosis. 2) Steroids should be used in early and evolving disease preferably within the first 72 hours of onset (to prevent widespread involvement) or during reappearance of erythema and/or necrosis on newly regenerated skin. However, we feel that once a large area of skin is uncovered, i.e. >20% of BSA, the advantages of the treatment would be far outweighed by its drawbacks. Dose and duration of steroid therapy is to be individualized. Oral prednisolone 1-2 mg/kg per day or parenteral steroid, either

dexamethasone 8-16 mg or equivalent hydrocortisone, is started and continued for 3-5 days followed by rapid tapering. Further, steroids have limited or no role in fully established cases of SJS/TEN with no new lesions. These cases should be managed with supportive and barrier nursing care.

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