Reviewing treatment of SJS in geriatric population; comparing combination of cyclosporine and steroid with use of steroid only.

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INTRODUCTION

Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are rare but life-threatening mucocutaneous diseases mainly caused by drugs [1] . Mortality seen with SJS is 1-5% and TEN is 25-35%.
SJS/TEN occur in all age group including infants and children. There is an increased incidence in the elderly, with relative higher mortality and morbidity.[2]
Beyond supportive care, there are no established systemic therapies for SJS and TEN. Studies regarding systemic medication provide mixed result.There is a lack of consesus regarding its appropriate management.
Use of cyclosporine was first introduced in literature by renfro et al in 1989 which show unprecedental result.[3]
Pathogensis of SJS-TEN[4]
•Epidermal keratinocyte apoptosis is the hallmark of SJS-TEN.

•Proposed by two mechanism:

1. cytotoxic T-cells are activated by an inciting drug, which leads to the release of granzyme B and perforin.

2.Fas-Fas ligand binding activates caspase 8, which results in nuclease activation and the widespread skin blistering characteristic of this severe drug reaction.

Mechanism of action of cyclosporine

•Cytotoxic T-cell, is blocked by cyclosporine: which plays a vital role in the pathogenesis of SJS/TEN.
•Calcineurin inhibition leads to reduced activity of the transcription factor
NFAT-1

•Inhibiting production of IL-2 .

•Inhibits IFN-γ production by T-lymphocytes

•Theoretically saying cyclosporine is a effective drug in the management of SJS-TEN.

Aim and objective of study:
To Review treatment of SJS in geriatric population and comparing combination of cyclosporine and steroid with use of steroid only.

Material and Method:
Case information was collected retrospectively of 8 patients admitted in skin ward of dermatology department in MDM hospital, SN medical college between year 2016 to 2019.
•Design : In this retrospective study, inclusion and exclusion criteria had been defined before any data extraction from the patients' medical records.
Inclusion

1.age>60

2.SJS diagnosed by dermatologist, biopsy proven
Exclusion criteria:
1. Previous treated with immuno modulator

2.Internal malignancy

3.Uncontrolled hypertension

4.Renal failure

5.Hypersensitivity to cyclosporine or any of its component.

Two groups of four patient were made : group A and B

Management of group A patients consisted of:
•Initial assessment
•Prompt withdrawal of offending drug
•Supportive treatment and investigation
•Initiation of dexamethsaone at a dose of 2mg/kg within 72 hrs and taper thereafter a week
•Cyclosporine 3-5mg/kg oral in divided dose till 7 to 14 days.

Management of group B

• Initial assesssment
•Prompt withdrawal of offending drug
•Supportive treatment and investigation
Dexamethasone dose of 2mg/kg is use as systemic therapy.

Result.

A total of 8 eight patients were included in the study with average age being 65.7

•Male and female ratio being 3:5

•In both the groups no mortality was observed.

•There was no side effect observed which warrant discontinuation of therapy.

Average duration of hospital stay in the group treated with cyclosporine and steroid being 8.7(SD=2.87) and of only steroid being 12(SD=4.8).

•Average time for stabilization of disease in patients treated with cyclosporine and steroid was 2 while in steroid alone was 3.5

•Complete reepithelization of skin in patients treated with cyclosporine and steroid take on average 6.5 days while on steroid only ,take 10 days.

Discussion

Several systemic treatment protocols for SJS-TEN is published; however none have been formally standardised in random control trial.

•Use of systemic steroid is controversial with mixed result. With recent study showing decrease in mortality(european study) or no change (REGISCAR study)with comparison to supportive treatment.

•Rationale for supra pharmacological high dose of dexamethasone followed by cyclosporine leads to modification of immune response, beside the side effect profile of steroid minimalize with interruption of progression.

•In a study by Singh et al., comparing cyclosporine-treated patients to a retrospective cohort of corticosteroid group found a significant decrease in the mean duration of reepithelialization ($P = 0.01$), stabilization, mean hospital stay ($P = 0.03$) and no mortality in the cyclosporine-treated group.

•IVIG is the most common immunomodulatory drug use for SJS-TEN in world. The cost of this drug make is largely inaccessible to large portion of geriatric population .

•A retrospective study by Kirchhof et al. comparing IVIG and cyclosporine showed a relative mortality benefit to the use of cyclosporine

Conclusion and Limitations.

The result in our case series provide evidence for shorter stay and earlier stabilization of disease in patients treated with cyclosporine and steroid. Its Results are consistent with other previous observation of research by Allan nore et al[5] , Singh et al [6]and wanjarus et al[7] .

•The results of this study are limited by their observational nature and small sample size from a single centre.

Reference:

1. Mockenhaupt M. The current understanding of Stevens-Johnson syndrome and toxic epidermal necrolysis. Expert Rev Clin Immunol. 2011;7:803–813.

2. Schwartz R, McDonough P, Lee B. Toxic epidermal necrolysis. Journal of the American Academy of Dermatology. 2013;69(2):187, e1-187, e16. https://doi.org/10.1016/j.jaad.2013.05.002.

3. Marcella P. Medeiros, Caroline H. C. Carvalho, Cláudia G. Santi, Joao Avancini, Stevens-Johnson syndrome and toxic epidermal necrolysis – retrospective review of cases in a high complexity hospital in Brazil, International Journal of Dermatology, 10.1111/ijd.14544, 59, 2, (191-196), (2019).

4. Downey A, Jackson C, Harun N, Cooper A. Toxic epidermal necrolysis: Review of pathogenesis and management. Journal of the American Academy of Dermatology. 2012;66(6):995–1003.

5. Valeyrie-Allanore L, Wolkenstein P, Brochard L, Ortonne N, Maître B, Revuz J, Bagot M, Roujeau JC. Open trial of ciclosporin treatment for Stevens-Johnson syndrome and toxic epidermal necrolysis. Br J Dermatol. 2010 Oct;163(4):847-53.

6. Singh G K, Chatterjee M, Verma R. Cyclosporine in Stevens Johnson syndrome and toxic epidermal necrolysis and retrospective comparison with systemic corticosteroid. Indian J Dermatol Venereol Leprol 2013;79:686-692.

7. Roongpisuthipong W, Prompongsa S, Klangjareonchai T. Retrospective Analysis of Corticosteroid Treatment in Stevens-Johnson Syndrome and/or Toxic Epidermal Necrolysis over a Period of 10 Years in Vajira Hospital, Navamindradhiraj University, Bangkok. Dermatol Res Pract. 2014;2014:237821.