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ORIGINAL ARTICLE

Efficacy of cyclosporine for the treatment of Stevens-Johnson syndrome and toxic epidermal necrolysis: Systemic review and meta-analysis

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ABSTRACT

Background: Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are life-threatening reactions, mainly to drug, characterized by epidermal necrosis and mucous membrane ulceration. SCORTEN-predicted mortality has been used to assess the efficacy of treatments comparing with actual mortality. Several literatures about cyclosporine have shown its ability to halt disease progression and decrease mortality.
Objectives: This study was aimed to provide a more evidence-based review by conducting a meta-analysis of cyclosporine for the treatment of SJS/TEN.
Methods: We conducted a systemic review of articles published before Jan 31, 2017. The outcomes were mortality rate and SCORTEN-based standardized mortality ratio (SMR). The pooled odds ratio (OR) and SMR ratio were analyzed from these extracted data.
Results: There were 7 observational controlled studies (1 historical controlled study) which met the inclusion criteria. The overall mortality rate for patients receiving cyclosporine was 7.1%. The observed mortality was significantly lower than predicted mortality in patients receiving cyclosporine (pooled SMR: 0.42; 95% CI, 0.19–0.95). The pooled estimate of ORs for 4 studies describing observed mortality in cyclosporine to intravenous immunoglobulins (IVIg) group was 0.40 (95%CI, 0.06–2.69). Comparison of SMR between cyclosporine and IVIg was presented with the pooled SMR ratio, which showed no significant difference in SMR ratio between two treatments (SMR ratio, 0.49, 95% CI, 0.08–2.89).
Conclusion: We have provided the first meta-analysis study regarding the efficacy on mortality of cyclosporine for treatment of SJS/TEN. From the existing research, cyclosporine has a beneficial effect on mortality. And there is a trend that cyclosporine demonstrated better survival whether in pooled OR or SMR ratio than IVIg. Due to the limitations of current studies, a double-blind randomized controlled trial is still urged.

Introduction

Stevens–Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are life-threatening conditions that arise as reactions to drugs. These conditions are characterized by epidermal necrosis and mucous membrane ulceration,[1] and their presentations are differentiated by the extent of body surface area (BSA) affected. Patients with less than 10% BSA involved are classified as having SJS, 10%–30% BSA as SJS/TEN overlap, and >30% BSA as TEN.[2] Although the incidence of these conditions is very low, the associated mortality rates are quite high, ranging from 1% to 5% in SJS and 25%–30% in TEN.[3] A prognostic scoring system, severity-of-illness score for TEN(SCORTEN), was developed and validated to predict mortality in patients with SJS or TEN,[4,5] and SCORTEN-based mortality rates have been used to assess the efficacy of treatments for these conditions.[6,7]

Conflicts of interest: The authors declare that they have no financial or non-financial conflicts of interest related to the subject matter or materials discussed in this article.

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Treatment for SJS and TEN is identification and withdrawal of the offending agent with supportive care. Systemic treatments, including systemic steroids, intravenous immunoglobulin (IVIg), and cyclosporine, have been studied for SJS and TEN. Due to an increased risk of complications associated with corticosteroid use,[8,9] treatment with IVIg or cyclosporine has increased among clinicians. Studies on the effect of IVIg on mortality rates have reported conflicting results[10,11]; however, several case reports and series on cyclosporine have reported its ability to halt disease progression and reduce mortality rates.[12–14] In this study, we conducted a meta-analysis and an evidence-based review on the effects of cyclosporine treatment on SJS/TEN.

Methods

Review protocol

Recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) statement, explanation and elaboration document, and checklists were followed as closely as possible to guide our methodology and reporting.[15]

Eligibility

We primarily focused our literature search on randomized controlled trials (RCTs); however, in the absence of randomized controlled trials, we included observational controlled studies that evaluated patients with ≥3 SJS, SJS/TEN overlap, or TEN receiving cyclosporine monotherapy. A controlled study was defined as a study that evaluated patients with ≥3 SJS, SJS/TEN overlap, or TEN receiving another kind of therapy within the same study. Review articles, letters, case reports, and conference reports were excluded. Articles that were not written in English were excluded."

Search strategy

We searched PubMed, MEDLINE, EmBase, and the Cochrane Library (including The Cochrane Database of Systematic Reviews, the Database of Abstracts of Reviews of Effects, The Cochrane Controlled Trials Register, and The Health Technology Assessment Databases) from their inception to Jan 31, 2017. All studies used for our analysis consisted of human clinical studies. The MeSH search headings included ("Stevens-Johnson syndrome "OR "toxic epidermis necrolysis") AND ("Cyclosporine" OR "Cyclosporin"). References within searched articles were also reviewed to identify potentially missed studies.

Study selection

The titles and abstracts of articles were first screened for eligibility by Y.T. Chen. The full texts of selected articles were independently reviewed by Y.T. Chen and Y.C. Huang. Articles irrelevant to our topic, based on title, abstract, and overall content were excluded. We also excluded articles without a full-text version of the

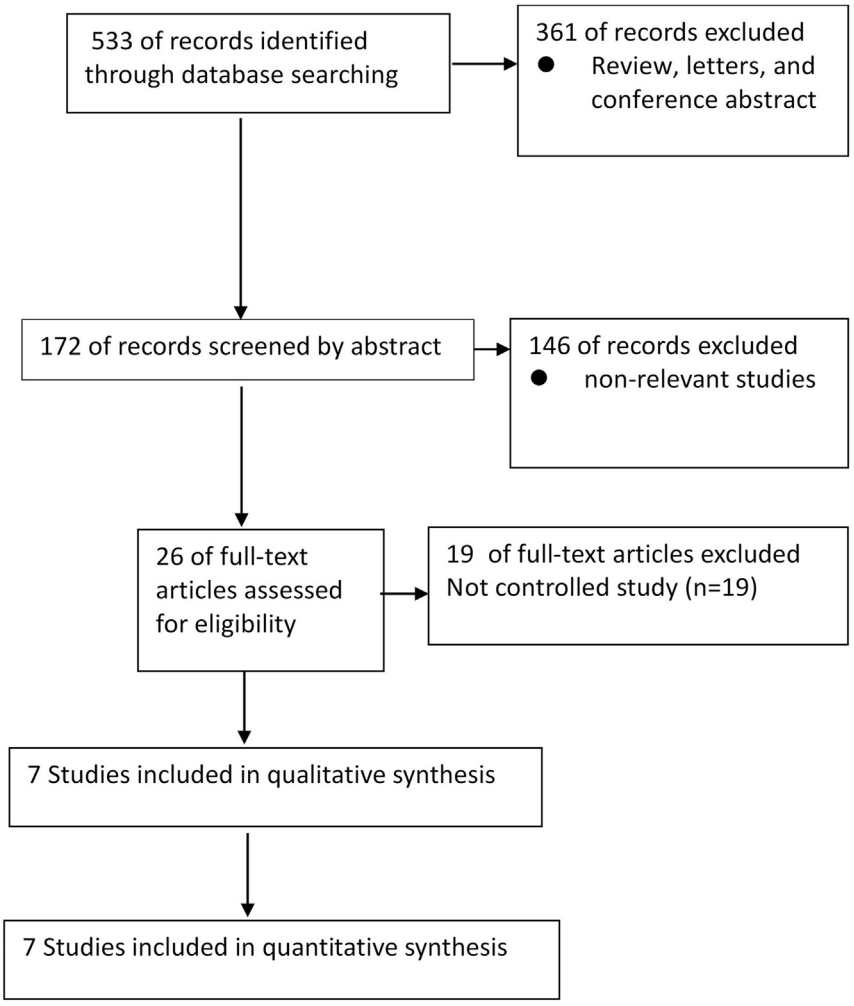

Fig. 1 The flow chart showed how the studies were selected. Seventy-six were initially identified through the initial search strategy. Consequently, 6 studies were included in this review.