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A systematic review and meta-analysis of case-control studies on cytokines in blister fluid and skin of patients with Stevens Johnson syndrome and toxic epidermal necrolysis

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ADMINISTRATIVE INFORMATION

Support - Nil.

Review Stage at time of this submission - The review has not yet started.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202420123

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 29 February 2024 and was last updated on 29 February 2024.

INTRODUCTION

Review question / Objective To determine whether the cytokine types and levels are different in blister fluid and skin tissue of patients with Stevens Johnson syndrome compared with controls (healthy skin, burns, other drug reactions e.g. erythema multiforme, other blistering diseases e.g. bullous pemphigoid).

Rationale The pathogenesis of Stevens Johnson syndrome and toxic epidermal necrolysis remains poorly understood and currently, the literature on this topic is conflicting. The dataset to be analysed is from a large burns referral centre in Australia. The principal and chief investigators both worked substantively in the dermatology department that produced the dataset.

Condition being studied Stevens Johnson syndrome; Toxic epidermal necrolysis.

METHODS

Search strategy Terms:
Gene expression or cytokines or inflammatory markers or chemokines or interleukins
AND
Stevens Johnson syndrome or toxic epidermal necrolysis or epidermal necrolysis or Lyell's syndrome or severe cutaneous adverse reactions

Electronic databases:
1. Pubmed
2. Embase
3. Scopus
4. Web of science.

Participant or population Adult patients with Stevens Johnson syndrome or toxic epidermal necrolysis.

Intervention Nil.

Comparator Healthy skin, burns, other blistering dermatoses (e.g. bullous pemphigoid), other drug reactions (e.g. erythema multiforme), lichen planus, other inflammatory and non-inflammatory dermatoses.

Study designs to be included Case control study.

Eligibility criteria Eligible studies were: (1) adult patients (2) Stevens Johnson syndrome and/or toxic epidermal necrolysis (3) blister fluid and/or skin tissue (4) case control design.

Information sources Electronic databases.

Main outcome(s) Cytokine (types and levels) in blister fluid and skin tissue of patients with Stevens Johnson syndrome and toxic epidermal necrolysis and controls (other blistering and non-blistering dermatoses).

Additional outcome(s) Nil.

Data management This systematic review will be conducted in accordance with the PRISMA guidelines. Data collection will be performed independently by two authors, with any disagreements regarding inclusion of citations being referred to a third author for mediation. Information will be collected using a standardised data collection form with the principal outcomes of interest being the types and levels of cytokines in blister fluid and skin tissue. If data from individual patients is not available, then the aggregate data will be collected.

Quality assessment / Risk of bias analysis Quality assessment/risk of bias will be assessed using the MIH quality assessment tool.

Strategy of data synthesis Following full-text screening, studies will be deemed eligible/ineligible for data extraction. The sample size for cytokines in blister fluid and/or skin tissue will be pooled and the cytokines reported in more than one study will be subjected to quantitative analysis. Statistical analyses will be performed with RStudio 4.3.1 (RStudio: Integrated Development for R. RStudio, PBC, Boston, MA URL http://www.rstudio.com/) using packages meta 6.5-0 (Schwarzer, 2023) and dmetar (Harrer et al. 2019). Meta-analysis for prevalence will be performed with metaprop function and presented as a Forest plot. A Funnel plot will be constructed to make a visual representation assessing whether small-study effects are present. Linear regression and Egger's tests will then be used to quantitatively assess for plot asymmetry.

Subgroup analysis Not applicable.

Sensitivity analysis Not applicable.

Language restriction English.

Country(ies) involved Australia/Australian.

Other relevant information Nil

Keywords Stevens Johnson syndrome, toxic epidermal necrolysis, blister fluid, skin tissue, cytokines, gene expression.

Dissemination plans Publish in a medical journal; Present at a medical conference.

Contributions of each author

Author 1 - Thomas Stewart - Define inclusion and exclusion criteria; Develop search strategy and locate studies; Select studies; Extract data; Disseminate findings.
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Author 2 - Nicole Seebacher - Define inclusion and exclusion criteria; Develop search strategy and locate studies; Select studies; Extract data; Disseminate findings.
Email: nsee6009@uni.sydney.edu.au
Author 3 - John Frew - Formulate the review question; Assess study quality; Analyze and interpret results; Disseminate findings.
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