INPLASY

Characteristics and Management of Generalized Bullous Fixed Drug Eruption (GBFDE): A Protocol for Systematic Review

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ADMINISTRATIVE INFORMATION

Support - No financial support or sponsor.

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

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 12 October 2024 and was last updated on 12 October 2024.

INTRODUCTION

Review question / Objective The aim of this systematic review is to determine the causative agents, clinical features (epidemiology, latency, risk factors), outcomes (complications, mortality rate) and treatment of Generalized Bullous Fixed Drug Eruption (GBFDE).

Rationale Generalized Bullous Fixed Drug Eruptions are one of many Severe Cutaneous Adverse Reactions delineated in the RegiSCAR project. While other SCARs are better understood, to date no systematic review of the clinical features, causes, outcomes and treatment of Generalized Bullous Fixed Drug Eruptions has been published.

Condition being studied Generalized Bullous Fixed Drug Eruption, the most severe form of Fixed Drug Eruption is characterized by widespread red or brown macules or plaques with overlying large flaccid bullae associated with systemic symptoms, such as fever, malaise, or arthralgias.

METHODS

Search strategy Terms: generalized AND bullous AND fixed AND drug AND eruption. Databases: Embase, Pubmed.

Participant or population All patients with Generalized Bullous Fixed Drug Eruption.

Intervention Nil.

Comparator Nil.

Study designs to be included Cohort studies, cross-sectional studies, case series, case reports.

Eligibility criteria Inclusion criteria: Original observational cases of GBFDE, defined by at least two (probable case) or three (definite case) of the following pre-defined criteria in a previous study using the RegiSCAR database:
i. similar reaction in the past;
ii. fewer than two mucous membranes involved, absence of spots or target lesions;

iii. large and well-demarcated blisters and erosions;
iv. the presence of lesions and erosions on at least two different sites of the body (a site being defined as part of the body area as used for the 'rule of nine' for estimating BSA) to distinguish generalized from localized forms of FDE

Exclusion criteria:
• Studies that do not include quantitative patient data
• Reviews that do not report original cases of GBFDE
• Studies that only cite previously published cases of GBFDE
• Cases cited from previously published studies
• Alternative types of cutaneous adverse reaction
• Cases not meeting the criteria for validation as described in the inclusion criteria
• Number of cases not clearly identified or able to be calculated
• Cases from studies with full text unavailable.

Information sources Electronic databases PubMed, Embase.

Main outcome(s) Causative agents of Generalised Bullous Fixed Drug Eruption (GBFDE).

Additional outcome(s)
1. Epidemiology of GBFDE
2. Latency period of GBFDE
3. Risk factors of GBFDE
4. Mortality rate of GBFDE
5. Complications of GBFDE (including but not limited to systemic involvement, organ dysfunction, high dependency or intensive care unit stay, length of stay in hospital, long term sequelae including scarring)
6. Treatment of GDFDE and efficacy rate.

Data management This systematic review will be conducted in accordance with PRISMA guidelines. The screening process including manual removal of duplicates found will be done by 1 author (LLY). This is followed by title and full abstract screening performed independently by 2 authors (LHY and LLY) manually by applying the inclusion and exclusion criteria. All full text publications assessed are checked independently again by the 2 authors and any inconsistencies between the authors discussed and resolved. A standardized excel spreadsheet will be used to record and manage data extraction according to the outcomes desired.

Quality assessment / Risk of bias analysis The Newcastle-Ottawa and modified Newcastle-Ottawa score will be used to assess the quality of included studies. Publication bias will be addressed by performing a comprehensive search strategy that includes multiple databases to ensure that all relevant cases are captured. We will also assess for evidence of publication bias using funnel plots if a meta-analysis of sufficient size can be performed. Selective reporting bias will be evaluated by comparing the outcomes reported across included case reports and case series. To avoid duplication bias, we will carefully cross-reference all included studies to identify potential duplicate publications of the same case. Studies with overlapping patient descriptions will be flagged, and duplicate data will be excluded from analysis. Any suspected duplicates will be verified through patient demographics and clinical details such as drug exposure and timeline of events.

Strategy of data synthesis Basic descriptive statistical analysis will be performed using GNU PSPP Software (Version 2.0.1). Where relevant, univariable logistic regression will be used to compare the outcomes between groups with different demographics and clinical features.

Subgroup analysis Nil.

Sensitivity analysis Nil.

Language restriction English.

Country(ies) involved Singapore.

Other relevant information Nil.

Keywords Generalised Bullous Fixed Drug Eruption.

Dissemination plans Publish in a medical journal, present at medical conferences.

Contributions of each author
Author 1 - Li Yang Loo - Define inclusion and exclusion criteria, develop search strategy and locate studies, select studies, extract data, analyse and interpret results, disseminate findings.
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Author 2 - Haur Yueh Lee - Define inclusion and exclusion criteria, develop search strategy and locate studies, select studies, extract data, analyse and interpret results, disseminate findings.
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