

INPLASY PROTOCOL

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Review Stage at time of this submission: Data analysis.

INTRODUCTION

Review question / Objective: To review articles, examine the incidence of grade 3 hyperglycemia in randomized controlled trials (RCTs), and assess possible causes of adverse events.

Effect of Sofosbuvir/Velpatasvir/Voxilaprevir Treatment on Serum Hyperglycemia in Hepatitis C Virus Infections: A Systematic Review and Meta-Analysis

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Condition being studied: Sofosbuvir, velpatasvir, and voxilaprevir (SOF/VEL/VOX) is an effective, safe rescue therapy regimen for patients have previously been treated failure. Initiating Direct-Acting Antiviral (DAA) treatment for HCV infection with diabetes have experienced hypoglycemia, it could improve insulin resistance due to clean HCV. However, some studies shown that SOF/VEL/VOX has Grade 3 hyperglycemia adverse events. This finding contradicts that other DAAs studies.

Information sources: PubMed, Cochrane Library, ClinicalKey, Embase, and MEDLINE electronic databases were searched from their inception until October 2021.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 24 December 2021 and was last updated on 19 April 2021 (registration number INPLASY2021120109).

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METHODS

Search strategy: Using Boolean operators and search terms without language or publication year restrictions. The search was not restricted to the published English-language articles and articles that were obtained by filtering RCTs and human subjects.

Participant or population: Hepatitis C patients who have previously failed a direct-acting antiviral (DAA) or naive experiences.

Intervention: SOF/VEL/VOX (Sofosbuvir/velpatasvir/voxilaprevir).

Comparator: Other DAAs regimens.

Study designs to be included: Inclusion criteria were randomized and SOF/VEL/VOX interventions reporting grade 3 hyperglycemia and sustained virologic response at post-treatment week 12 for HCV infection. Using Boolean operators and search terms without language or publication year restrictions. The search was not restricted to the published English-language articles and articles that were obtained by filtering RCTs and human subjects.

Eligibility criteria: Retrieved articles were included in the review if: (1) they described SVR12 and relapse states after treatment with SOF/VEL/VOX for HCV infection; (2) the safety outcomes recorded consisted of grade 3 serum glucose parameters; and (3) data on other grade 3 laboratory abnormalities (adverse events) were present. Study eligibility was based on initial screening of titles, methodologies, and abstracts, followed by full-text reviews.

Information sources: PubMed, Cochrane Library, ClinicalKey, Embase, and MEDLINE

electronic databases were searched from their inception until October 2021.

Main outcome(s): The primary outcome was grade 3 hyperglycemia defined as serum glucose levels >250 mg/dL.

Additional outcome(s): The secondary outcome was to discriminate the risk factors of the event, and other grade 3 laboratory abnormalities were documented.

Quality assessment / Risk of bias analysis: The study was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines; quality assessment was performed using the Cochrane risk-of-bias tool for RCTs.

Strategy of data synthesis: This research contained integrated data from the available articles. A random-effects model was employed to pool data. Findings were presented as risk ratios (RRs) with 95% confidence intervals (CIs).

Subgroup analysis: Subgroup analyses by exposure duration of treatment, HCV genotype infections, and patients who have previously been treated with DAA.

Sensitivity analysis: We also conducted sensitivity analyses to explore the impact of heterogeneity within our analysis. After removing studies that had a high risk of bias, we repeated our analyses by using fixed-effects models. All analyses were performed by using random-effects meta-analysis models with OpenMeta[Analyst] software (Center for Evidence-Based Medicine, Brown University, Rhode Island, USA).

Country(ies) involved: Taiwan.

Keywords: Hyperglycemia, SOF/VEL/VOX, Hepatitis C, Diabetes.

Contributions of each author:

Author 1 - Hsuan-Yu Hung had contributions to the conception, design of research, the acquisition, analysis, and interpretation of data for the study.

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Conflicts of interest: Hsuan-Yu Hung has received research support from Ditmanson Medical Foundation Chia-Yi Christian Hospital. All authors have no competing interests to declare that are relevant to the content of this article.