

Name of journal: World Journal of Critical Care Medicine

ESPS Manuscript NO: 14432

Reviewed by 02474355

Gupta and Colleagues from the Department of Intensive Care Medicine, Frankston Hospital, Frankston, Frankston, Australia review heparin induced thrombocytopenia syndrome (HITS), a distinct entity that is characterised by the occurrence of thrombocytopenia in conjunction with thrombotic manifestations after exposure to unfractionated heparin or low molecular weight heparin. It is an immunologic disorder mediated by antibodies to Heparin-platelet factor 4 (PF4) complex. HITS is an uncommon cause of thrombocytopenia. The reported incidence of HITS in patients exposed to Heparin varies from 0.2% to upto 5% and in ICU populations, the estimates vary from 0.39% - 0.48%. In this excellent review the incidence, pathogenesis, diagnosis and management of HITS are discussed. The Authors conclude that the diagnosis of HITs in critically ill patients requires early recognition for successful management. Exclusion of other causes for thrombocytopenia and or thrombosis with special consideration to the temporal relationship of onset of thrombocytopenia with exposure to UFH/LMWH is vital. Use of clinical pretest probability scores such as 4T score in conjunction with more specific assays such as anti-IgG heparin PF4 antibody may reduce over-diagnosis of the disease. Tables and Figures are informative except Figure 2 that should be made more readable. The Reference list is up-to-date and comprehensive.

Authors Response: Thank you for reviewing our manuscript. We have modified Figure 2 as per your suggestion.

Reviewed by 02458171

The authors discuss the incidence, pathogenesis, diagnosis and management of Heparin induced thrombocytopenia syndrome (HITS) in the context of latest available information from relevant scientific articles and present their view on the HITS using appropriate scientific information. Since heparin-induced thrombocytopenia is a major problem in the treatment of seriously ill patients, so the information is relevant to a wide range of doctors, and can be useful in clinical practice. I recommend authors: 1) to arrange corrections in abstract by starting abstract with the last sentence "In this review we discuss the incidence, pathogenesis, diagnosis and management of HITS" and 2) to change the font in Figure 2, because the content of the image is hard to read.

Authors Response: Thank you for reviewing our manuscript. We have modified the abstract and figure 2 as per your suggestions

Reviewed by 01991880

The review by Gupta et al. covers many aspects of diagnostic, clinical and therapeutical management of HIT. The manuscript does not contain errors and provides the reader with sufficient informations on this issue. However, although formally correct, the review does not add any new information on this clinical setting. Moreover, recent data on the same issue were not cited under References (e.g. Crowther et al. J Crit Care. 2014 Jun;29(3):470.e7-15). Thus, the manuscript looks like a valuable repetition of analogous reviews on this disorder and does not give particular details on the management of HIT occurring in critically ill patients. This aspect considerably weakens the manuscript and its clinical relevance. Minor comments Figure 2 is not graphically clear and thus cannot be easily read. The characters of the text should be significantly enlarged.

Authors Response: Thank you for your review of our manuscript. The study by Crowther that you suggested was not published when we wrote this review. This study as such is not a review but was performed with an aim to evaluate whether a published clinical prediction rule (the "4Ts score") reliably rules out HIT in "low-risk" intensive care unit (ICU) patients as assessed by research coordinators. We have modified figure as per your suggstions.