

Do not exclude glucarpidase too soon in the context of high-dose methotrexate induced nephrotoxicity

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To the Editor,

We read with interest the article 'Glucarpidase treatment for methotrexate intoxication: a case report and review of literature' by Boelens et al.¹ We would like to address some concerns of the authors.

As the authors correctly state, methotrexate (MTX) induced acute kidney injury (AKI) has the potential to induce a vicious circle in which delayed clearance maintains high systemic MTX levels, causing further kidney damage. Glucarpidase reduces plasma MTX concentrations by > 95% within 15 minutes of administration and is by far superior to extracorporeal techniques in removing MTX effectively from the circulation.

In the recently published 'Consensus guideline for use of glucarpidase in patients with high-dose MTX induced acute kidney injury and delayed methotrexate clearance' by Ramsey et al., a more detailed recommendation for glucarpidase therapy is defined,² compared with the original recommendations for use at the time of FDA approval.³ Both high plasma MTX concentrations at several points after the start of high-dose MTX infusion and the 24-hour serum creatinine concentration are taken into account (a significant elevation (> 1.5) above baseline level). The expert panel concluded that administration of glucarpidase should optimally occur within 48-60 hours from the start of the high-dose MTX infusion, because

life-threatening toxicities may not be preventable beyond this point. In the case Boelens et al. describe, the patient received glucarpidase after 85 hours. Clearly, a tighter time schedule necessitates prompt access to glucarpidase.

At the moment of writing, glucarpidase is not registered for use in Europe and hospital pharmacies are not allowed to keep it in stock. This is also the case for several other antidotes. Commissioned by the Ministry of Health (VWS) of the Netherlands, and in cooperation with the Dutch Poisons Information Center (NVIC/UMC Utrecht) a national antidote stock is set up at the National Institute for Public Health and the Environment (RIVM) in 2018. Several rarely used, non-registered and often very expensive antidotes, including glucarpidase, are kept in stock, making these antidotes quickly available in case of medical emergencies. For more information on antidote availability contact the NVIC.

REFERENCES

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