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Renal Safety Of Zoledronic Acid In Patients With Borderline Kidney Function At A Metabolic Bone Centre In The United Kingdom

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Abstract

Background:

Zoledronic acid is a bisphosphonate widely used for the treatment of osteoporosis that leads to improvements in bone mineral density and reductions in fractures. A potential side effect is nephrotoxicity and acute kidney injury (AKI). Advice from the UK Medicines and Healthcare products Regulatory Agency (MHRA) in 2019 stated that creatinine clearance (CrCl) and not estimated glomerular rate (eGFR) should be used to guide and make decisions about treatment and that patients should not receive zoledronic acid if their CrCl is below 35 ml/min. The objective of this study was to review the safety of our previous practice using eGFR and the clinical impact of implementing the MHRA recommendations.

Methods:

The study was performed at the Metabolic Bone Centre (MBC) in Sheffield Teaching Hospitals, UK. Data on all the patients who had zoledronic acid infusions from the 1/09/2015 to the 1/10/2020 at the centre were retrieved and evaluated.

Results:

Data on 4405 patients were retrieved. Serum creatinine in the 14 days post- infusion was available for a total of 969 infusions and amongst them, 160 (16%) infusions were given with baseline CrCl < 35 ml/min. AKI was observed within 14 days following 45

infusions (4.5%). Only 9 infusions resulted in AKI with a pre-treatment of CrCl < 35 ml/min.

If the MHRA rules had been followed (calculating CrCl for patients aged ≥75years and/or extreme BMI <18 or >40 kg/m^2), 996 infusions with baseline CrCl<35 ml/min would not have been given.

Logistic regression showed that both CrCl and eGFR were significant factors in predicting AKI within 14 days, but that the current recommended cut-off of CrCl 35 ml/min had a poor sensitivity. The areas under the curve for each marker were 0.608 and 0.627 respectively, suggesting that neither are sensitive in predicting AKI.

Conclusions:

This study suggested that zoledronic acid could be contributing to the development of AKI in some patients. Estimated GFR is better validated that CrCl and so is preferable to use. Since low eGFR is at least as good a predictor of AKI as CrCl, it should be used in every day clinical practice.

Conflicts of Interest

MS receives consultancy from Kyowa Kirin International and grant funding from Roche Diagnostics

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