PPIs and hypomagnesaemia: more common than we thought?

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Proton pump inhibitors (PPIs) are associated with several well-documented side-effects but one emerging adverse effect, hypomagnesaemia, has so far tended to slip under the radar. In a small audit, the author investigated the rates of magnesium supplementation among PPI users, as a potential indicator of hypomagnesaemia. The results suggest this side-effect could be more common than previously thought.

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While PPIs are highly effective and generally well tolerated, warning signals emerged over 10 years ago regarding possible adverse effects that included an increased risk of fractures, pneumonia, enteric infections and vitamin B₁₂ deficiency. Over the last decade, our knowledge of these potential harms has expanded and although some reviewers have concluded that associations may be explained by confounding, other work supports the legitimacy of the earlier safety signals.

Studies have also emerged more recently reporting other possible serious consequences of PPI use, such as an association with myocardial infarction (MI) and dementia. However, further research in these areas is required, to inform our understanding and consequently clarify whether there is a need for us to change PPI prescribing practices.

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PPIs and hypomagnesaemia

While reports about MI and dementia even reached the lay media, another emerging PPI-related adverse effect, hypomagnesaemia, has tended to slip under the radar, even for many health professionals. This is despite a steadily growing number of reports, some detailing serious consequences. Perhaps this is because a number of things set hypomagnesaemia apart from some of the other potential adverse effects linked to PPIs. One is that the typical symptoms of magnesium deficiency are nonspecific and may have an insidious onset. Secondly, that patients developing symptoms such as muscle cramps may self-medicate with a supplement, either after consulting ‘Dr Google’ or seeking the advice of a pharmacist or naturopath. Thirdly, serum magnesium levels may not be part of the standard panel of biochemistry tests undertaken and so hypomagnesaemia may not be formally diagnosed.

These issues have become particularly apparent to me while conducting comprehensive medication reviews in patients’ homes. Spending typically an hour with each patient enables a thor-
ough medication history to be taken, which includes use of over-the-counter, complementary and alternative medications. While the patients I see invariably obtain their PPI on prescription, it is of course worth noting that PPIs are now available over the counter and so in some cases GPs may be unaware that patients are self-medicating with these drugs. A home medicines review may also reveal the presence of bothersome symptoms (eg cramp) that, in some cases, have not been brought to the attention of the GP.

Audit of magnesium supplementation

Magnesium products are now among the supplements most commonly used by the patients I see and this has prompted me to carry out an audit of the last one hundred medication reviews I have undertaken. This revealed that 55 patients (55%) were currently taking a PPI and of these, 14 (25.5%) were also taking a magnesium supplement, in contrast to eight patients (17.8%) among those not taking a PPI. Among the 14 patients taking a PPI and magnesium, use of the supplement was not recorded on the GP’s medication profile for seven (50%) of these. In 10 (71.4%) of those taking a PPI and magnesium, the medication review recommendations to the GP included a PPI step-down, based on the indication for the PPI, the patient’s gastrointestinal symptoms, comorbidities, concurrent medications and the relevance of one or more potential PPI adverse effects for the patient.

With such a small sample, the observed difference in rates of supplementation between PPI users and non-users is not statistically significant. However, based on this audit, a larger study is now planned. This will take into account other potential influences, such as use of diuretics, which may not only contribute independently to hypomagnesaemia, but also increase the risk of this problem when they are used concurrently with a PPI.19

In the meantime, it appears there may be a place for clinicians to weave hypomagnesaemia into their discussions with patients surrounding the pros and cons of PPI therapy and, where clinically appropriate, the opportunities to step-down therapy.

References

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