

A commentary on operamide and cardiotoxicity

To the Editor,

The Letter uncovers an issue which is increasingly relevant in Community Hospital practice.

The authors have highlighted the following points with an interesting case and adequate referencing, but the points are relatively well reported and not novel.

There has been a clearly documented increase in the number of reported cases of loperamide abuse and toxicity in the literature in recent years. There is a relatively clear established link between loperamide use and cardiotoxicity. The cardiotoxic effects more commonly reported include QTc prolongation and QRS interval prolongation with concomitant ventricular arrhythmias. There has also been an increase in popular awareness regarding the abuse potential of loperamide which has entered the public domain. The increased abuse of loperamide may be related to the general trend of restricting prescriptions of controlled substances

A few additional points that may be brought to the authors attention:

- (1) This is a nationwide issue. There are reports stemming from all across the country. The authors have mentioned data extracted from the California Poison Control Database. In 2016, Bishop-Freeman et al. [1] published an account of cases from North Carolina as well.
- (2) There may be a dose-response relationship between loperamide abuse and cardiotoxicity. The levels of the drug in reports have been far higher than those recommended for anti-diarrheal use, but there is no clear consensus on a definite level at which adverse effects appear.
- (3) Miller et al. [2] published a comprehensive review this year, which I encourage the authors to go through in order to add to their report. They mention two interesting points regarding the epidemiology. First, there has been a sharp rise in loperamide toxicity case reports arising out of its use as an opiate substitute rather than as an anti-diarrheal since 2014 and secondly, the use of loperamide in conjunction with other medica-

tions reported in toxicity cases has also increased.

- (4) There is a well-researched association between P-GP receptor inhibitors being administered together which may contribute to both increased loperamide serum concentration and adverse reactions. It is not well known if this also contributes to increased euphoric effect and abuse potential, but it has been mentioned in opiate user support group websites that it can be used for withdrawal symptoms concomitantly with cimetidine or grapefruit juice.
- (5) Treatment for this condition is mainly supportive and- in addition to the various therapies mentioned by the authors- intravenous isoproterenol, transcutaneous electrical pacing, and transvenous pacing have also been used.
- (6) The authors have mentioned correctly that naloxone has been used and found useful to treat respiratory depression, but must add that it has no known effect on the arrhythmias.

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Disclosure statement

No potential conflict of interest was reported by the author.

References

- [1] Bishop-Freeman SC, Feaster MS, Beal J, et al. Loperamide-related deaths in North Carolina. *J Anal Toxicol.* 2016;40:677–686.
- [2] Miller H, Panahi L, Tapia D, et al., Loperamide misuse and abuse. *J Am Pharm Assoc.* 2017 Mar–Apr;57(2S): S45–S50.