

## The domperidone dilemma in Pakistan: Balancing access and safety concerns

Ahmed Umer, Zain Ul Hassan, Mamin Mehboob

Dear Madam, Domperidone is used in the treatment of nausea and vomiting as an antiemetic and prokinetic drug. Its pro-kinetic effects mainly manifest in the upper gastrointestinal tract by acting as a dopamine receptor antagonist.<sup>1</sup> However, the drug has been banned by the FDA in the USA due to its association with cardiac arrhythmias and cardiac arrest. A recent meta-analysis has shown a statistically significant association between sudden cardiac death<sup>2</sup> and the use of domperidone which raises the question of drug usage in Pakistan as an over-the-counter medication.

The meta-analysis considers six different case-control studies, between 2005 and 2016, that have shown an increase in the risk of sudden cardiac death and ventricular arrhythmias associated with domperidone. The observational studies were conducted in North America, Asia, and Europe, proving that it is a global phenomenon, stemming from the use of the drug. The forest plot of the studies has been mentioned later in the abstract showing heterogeneity at 0%, OR ratio 1.69 with 95% CI (1.46-1.95).

To further highlight the risks associated with domperidone, another study has reported that the safety index of the drug is 5.25, which is remarkably lower than the international safety ratio of 30.<sup>3</sup> The safety index, or therapeutic index, is the ratio of the toxic dose in 50% of the population (TD50) and the effective dose in 50% of the population (ED50) with the same therapeutic effect. A wider safety index indicates more room for error in the drug's therapeutic effect; essentially a larger barrier before the drug is toxic. With a safety index of 5.25, the action potential duration is markedly increased, resulting in arrhythmias. The author also comments on restricting the drug only to patients where the potential benefit is proven to justify the risks.

2nd Year MBBS Student, Ziauddin Medical College, Karachi, Pakistan.

**Correspondence:** Ahmed Umer. e-mail: ahmedumersheikh2000@gmail.com

ORCID ID: 0009-0008-2594-8435

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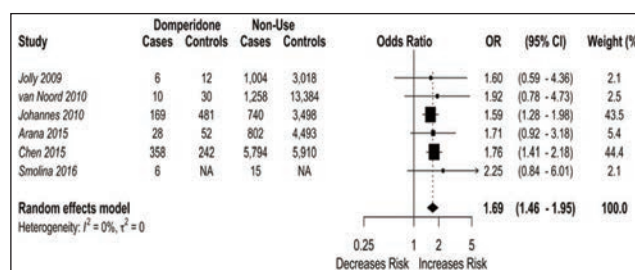
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**Figure:** Forest plot of the association of domperidone and the risks of sudden cardiac death and ventricular arrhythmias (reproduced with permission from reference 2).

In Pakistan, Domperidone is readily available as an over-the-counter drug. The casual availability raises the concern that the associated safety issues must be critically evaluated to determine whether the uses of the drug outweigh the risk of sudden cardiac death and ventricular arrhythmias<sup>4</sup> mentioned in these studies.

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