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Citation: Freedman, S., et al. "Ondansetron and the Risk of Cardiac Arrhythmias: A Systematic Review and Postmarketing Analysis." *Annals of Emergency Medicine.* 2014; Vol 64: 19-25.
Clinical Question: Is single dose oral ondansetron associated with increased risk of cardiac arrhythmias?
Background: In 2011, the FDA issued a warning that Zofran may induce fatal arrhythmias. In June 2012, FDA published an updated warning that 32 mg IV Zofran may increase the risk of QT prolongation. Current guidelines recommend avoiding Zofran in patients with congenital long-QT syndrome and screening with EKG and BMP prior to administration in high-risk patients (e.g. CHF, bradyarrhythmias, known electrolyte abnormalities, etc).
Methods: This was a systematic review covering published literature, Grey Literature, manufacturer's database, FDA Adverse Events Reporting System, and the WHO Individual Safety Case Reports Database. Cases included in the study had documented cardiac arrhythmia within 24 hours of oral Zofran administration. Primary outcome was arrhythmia associated with administration of single dose of oral Zofran. Secondary outcome addressed arrhythmias associated with Zofran irrespective of dose, frequency, or route.
Results: After screening and exclusions, a total of eleven (18%) pediatric and 49 (82%) adult cases were included for review. Primary outcomes demonstrated no reports of arrhythmia associated with single oral dose of Zofran. Secondary outcomes demonstrated 48 of these cases (80%) involved IV administration and 2 (3%) involved long term oral Zofran use in patients previously known to have multiple arrhythmia risk factors. 83% of these patients were found to have significant past medical history or on other medications know to have QT-prolongation side effects, particularly chemo drugs.
Discussion/Limitations: Authors conclude that routine EKGs and electrolyte screening prior to administration of oral Zofran is not indicated however appropriate measures should be considered in high-risk patients and those receiving IV Zofran. Given this was a systematic review, the only data available comes from reported cases, which is a major limitation. There is also an issue of sited causality. Were the reported arrhythmias caused by Zofran or the underlying baseline conditions/concomitant QT prolonging medications? Interestingly, the authors estimated that approximately 16,000 screening EKGs would need to be performed in order to identify a single asymptomatic long-QT syndrome, which would amount to approximately $5.5 million per 1 true case. In addition to exorbitant costs associated with aggressive universal screening, this leads to delays in ED flow and compromises resource utilization.
Bottom line: Oral Zofran is highly unlikely to induce fatal cardiac arrhythmias. Appropriate risk stratification and cost/benefit analysis should guide decisions on screening patients prior to administration of IV Zofran. Be cognizant of the side effects and potential risk factors in your patients.