Letters to the Editor

Can we prevent ondansetron induced fatal ventricular tachycardia?

Sir,

We have read with interest the article ‘Ondansetron induced fatal ventricular tachycardia’ by Chandrakala et al., published in the Indian Journal of Pharmacology, August 2008. We would like you to give us the opportunity to discuss some of our observations on the same.

Ondansetron is a racemic compound having one chiral centre. Racemic Ondansetron is a 50:50 mixture of two enantiomers, R-Ondansetron and S-Ondansetron. In one animal study (in dogs), effects of R-Ondansetron, S-Ondansetron and racemic Ondansetron on cardiac arrhythmias (cardiotoxicity) were evaluated. QTc interval was most prolonged among animals receiving S-Ondansetron and racemic Ondansetron and was shortest among animals receiving R-Ondansetron. Based on these results it was reported that R-Ondansetron has less cardiotoxicity than S-Ondansetron or racemic Ondansetron.[1]

Bodhankar et al. in 2006 studied the effect of racemic Ondansetron, R-Ondansetron and S-Ondansetron on QTc interval in electrocardiograms of rats. The Ondansetron and its enantiomers were administered IV in a dose of 3 mg/Kg and changes in QT and RR interval and heart rate were calculated. The results of this study showed that racemic Ondansetron and S-Ondansetron significantly prolonged QTc interval, while
R-Ondansetron did not prolong QTc interval as compared to the vehicle treated group. They concluded that R-Ondansetron is safer on the heart. Authors reported that S-Ondansetron might have higher inhibitory effects on Bezold-Jarisch reflex and this might be the reason for QTc prolongation with S-Ondansetron and racemic Ondansetron.  

A multicentric, randomized, double-blind, parallel group, comparative study on efficacy and safety of R-Ondansetron 4 mg versus racemic Ondansetron 8 mg in 240 Indian patients with nausea and vomiting concluded that R-Ondansetron 4 mg BID was equally effective compared to racemic Ondansetron 8 mg BID with a slightly better safety profile compared to racemic Ondansetron. This suggests that the S-Ondansetron component can be omitted without loss of efficacy. Efficacy and safety of R-Ondansetron solution was also studied in 410 pediatric patients confirming R-Ondansetron solution is safe and effective in pediatric patients with nausea and vomiting.

From the above discussion it is clear that R-Ondansetron 4 mg alone is sufficient for its anti-emetic potential and is preferable without its counterpart – the S-isomer which can prolong the QTc. So switching from racemic Ondansetron to R-Ondansetron is a rational therapeutic approach. R-Ondansetron has been approved by the DCGI on 15th April 2005 and is available as tablets (2 mg/4 mg), solution (1 mg/5 ml) and injection (1 mg/ml).

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References