Letters to Editor

Cardiac arrest associated with ranitidine and ondansetron combination in day care gynecologic surgery

Sir,

Day care surgery has become increasingly popular because of its cost-saving potential. However, the occurrence of post-operative nausea and vomiting (PONV) can delay patient discharge. Ranitidine and ondansetron are commonly used as a premedication to reduce the chances of PONV. Herein, we present a case to emphasize a rare but serious cardiovascular side-effect probably caused by ranitidine and ondansetron combination.

A 38-year-old female patient was admitted for medical termination of pregnancy and laparoscopic tubal ligation in day care surgery unit. Her pre-anesthetic check-up was normal. All routine investigations were in normal limits and electrocardiography (ECG) showed a sinus rhythm. Pre-operatively her heart rate was 82 beats/min and blood pressure 120/76 mmHg. Patient was pre-medicated with ranitidine 50 mg intramuscularly 45 min before surgery. In operating room, all standard monitoring were attached. Before administration of ondansetron, heart rate and blood pressure were 76/min and 116/80 mmHg. She was given ondansetron 4 mg intravenously, slowly over 30 s. However within 30 s of administering the drug, she became unresponsive to stimuli, apneic and ECG showed flat line and no peripheral or central pulse could be palpated. Cardio pulmonary resuscitation (CPR) was started. Immediately, we intubated the trachea with 7.5 mmID cuffed endotracheal tube. Within 2 min of CPR and administration of atropine 0.6 mg, there was return of spontaneous circulation and the monitor showed a normal sinus rhythm with a heart rate of 96/min and blood pressure 132/80 mmHg. Subsequently, spontaneous respiratory efforts returned in the next 2 min. After observing her for another 5 min and ascertaining that she had adequate spontaneous respiratory efforts and oxygen saturation, trachea was extubated. She was awake, oriented, with no neurological deficit and had stable hemodynamics. Surgery was performed after 48 h and was uneventful. This time however she was pre-medicated with i.v. metoclopramide 10 mg 1 h prior to the procedure.

The maximum effect of intramuscularly ranitidine occurs approximately after 45 min and this is the time when we administered ondansetron i.v., so it is presumed that it may be due to combined effect or ondansetron alone. Ondansetron...
has rare cardiovascular adverse effects such as atrial fibrillation, bigeminy, sinus bradycardia, ventricular tachycardia, QT prolongation, cardiac arrest.\textsuperscript{1,2} Bradycardia and cardiac arrest (asystole)\textsuperscript{3} is also reported with ranitidine.

The adverse cardiac effects of ranitidine may be due to H\textsubscript{2} receptor antagonism in coronary smooth muscle, through vasoconstriction or a rise in plasma histamine levels.\textsuperscript{4} Other mechanisms may include a cholinergic action mediated by cholinesterase inhibition.

Ondansetron has submicromolecular affinity for K + channels encoded by “human ether-a-go-go related gene,” which is possibly responsible for the prolongation of cardiac repolarization, thus resulting in conduction disturbances like QT/QTc interval prolongation.\textsuperscript{5} Presence of 5-hydroxytryptamine (5-HT) receptors in left ventricle usually precipitate the von Bezold Jarisch reflex and use of 5-HT\textsubscript{3} antagonist usually block this effect. However, the cardiovascular effect of ondansetron will depend on pre-existing serotonergic activity in both arms of the autonomic nervous system. The additional finding that this hemodynamic response was reversed by atropine emphasizes its likely parasympathomimetic origin.

The mechanism of cardiac arrest in this case is not clear either it is due to the combination of drug or ondansetron alone. Ondansetron and ranitidine both can cause bradycardia and cardiac arrest, so one should be careful when using the combination of two drugs.

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