Case Report

Double edged sword cardiac side effect of Ondansetron

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Sudden onset of bradycardia is not uncommon during the intra-operative period under anesthesia. It can be due to deeper planes of anesthesia, high spinal anesthesia, a surgical stimulus of the parasympathetic system, already existing cardiac disease, treatment with beta-blockers or use of intraoperative drugs like Clonidine, Dexmedetomidine. Ondansetron has been reported to cause cardiac arrhythmia as especially in patients with QT prolongation. Only a few case reports are published where Ondansetron has resulted in bradycardia. Here we are reporting the sixth case of Ondansetron induced sudden onset of severe bradycardia which when treated resulted in atrial and ventricular ectopics with hypertension in 25yr old female patient who came for elective Lower Segment Caesarean Section (LSCS).

Key Words: *Ondansetron, Bradycardia, 5HT-3 receptor antagonist, Cardiac effect*

Ondansetron is a 5HT-3 receptor antagonist routinely administered for the treatment of postoperative nausea and vomiting. Cardiovascular side effects like atrial fibrillation, ventricular tachycardia, cardiac dysrhythmias, ventricular fibrillation resulting in mortality have been reported [1-3]. We report a rare cardiac adverse event of intravenous Ondansetron which presented as severe bradycardia and when treated produced atrial and ventricular ectopics and hypertension.

CASE HISTORY

A 25year old female with gravid 2, Para 1 with previous LSCS was electively posted for LSCS. She is a known case of systemic lupus erythematosus (SLE) for 2yrs with no history suggestive of cardiac involvement, was on treatment with oral tablets of Hydroxychloroquine and Prednisolone. Pre-operative blood investigations and vitals were within normal limits. After intravenous (IV) cannulation with 18G Ringer Lactate (RL) was started. The patient was anxious as she had a painful experience of spinal anesthesia (SA) for the previous surgery. After taking consent and reassuring the patient, she was positioned in the left lateral and SA was given with 0.5% heavy Bupivacaine 2ml at L3-L4 interspace with 26G Quincke needle. Co-loading with RL 500ml and left lateral tilt with a wedge was given. Level of sensory blockade was up to fourth thoracic dermatome (T4) level and the patient was hemodynamically stable. Patient complained of shivering which was managed with oxygen through facemask at a rate of 5L/min and IV Tramadol 30mg.To prevent nausea and vomiting, IV Ondansetron 4mg was given as practiced prophylactically. Patient became restless and the heart rate suddenly dropped to 30-35bpm IV Atropine 0.6mg was given. Heart rate picked up to 130-140bpm but the patient became more restless and complained of headache. ECG started showing atrial and ventricular ectopics. After reassuring the patient IV Lignocaine 60mg was given. Patients heart rate settled to 110-120bpm with BP of 170-180/100mmHg but the ectopics persisted. As the patient was hemodynamically stable, the surgeon was allowed to proceed with the surgery. IV Lignocaine 40mg was repeated as the changes in ECG persisted. Following which the ectopics disappeared and sinus rhythm was restored on ECG monitor. IV Paracetamol was given for the headache. Further, intra-operative course of the surgery was uneventful. Patient was shifted to high-risk labor room for monitoring, where the ECG taken was normal.

DISCUSSION

Ondansetron is the most common serotonin antagonist used for the prevention of nausea and vomiting1. The cardiac side effects of this drug reported are few. It's known to cause supraventricular tachycardia, premature ventricular contractions, myocardial infarction, ECG changes such as ST depression and prolongation of QT interval as it blocks the repolarizing action of serotonin. Kasinath et al reported atrial fibrillation within 15 min of intravenous administration of Ondansetron [1]. Bigeminy with ST segment depression and sinus bradycardia followed by functional rhythm with ventricular escape beats was reported by Baguleyet al [2]. In 2009 Afonso et al [4] had two cases in which Ondansetron reported to cause severe bradycardia with respiratory arrest and loss of consciousness [4]. Its cardiovascular action is mediated by blocking the HERG (Human ether a-go-go related gene) coated k+ channels leads to prolongation of QT interval and results in arrhythmias [3]. By prolongation of the final repolarization and action potential plateau phase, it can end up causing bradycardia also [2]. Bezold-jarish reflex which consists of hypotension, bradycardia, and apnea is mediated through serotonin. 5HT-3 receptor antagonism results in blockade of Bezold-Jarish reflex causing tachyarrhythmias. Unopposed action of other 5HT receptors when 5HT3 gets blocked can produce hypertension and tachyarrythmias1. The varying action on 5HT3 receptor is based on the pre-existing serotonergic activity on the autonomic nervous system [2].

Serotonin (5-Hydroxy tryptamine) known to cause an increase in heart rate, increase in force of contraction of heart, fibrosis of heart valves, coronary constriction, thrombus and arrhythmias through the 5HT receptors present in the heart [2]. Pro-arrhythmic action of serotonin is due to its action on L-type calcium channels and simultaneous action on potassium channels causing prolonged after depolarization and plateau phase in cardiac action potential. Recent studies show serotonin's action in intracellular proteins in the heart and production of serotonin in cardiac mast cells, myocytes and immunocytes as well[5].

CONCLUSION

In this patient, we strongly believe that Ondansetron is the reason behind sudden onset of bradycardia because even though the patient had SLE she was not having any symptoms of cardiac involvement of the disease. She was taking Hydroxychloroquine which is not known to have any cardiac side effect. Bradycardia due to high spinal was also ruled out because the patient's blood pressure was normal, the sensory level was till T4 and she didn't have any breathing difficulty. But the uniqueness of this case was that when bradycardia was treated with atropine it resulted in atrial and ventricular ectopics with hypertension. The recommended protocol for intravenous Ondansetron is to administer undiluted in not less than 30seconds, preferably over 2-5 minutes as instructed by the manufacturers which may help to detect and preventing sudden changes in the heart rate and other adverse effects due to Ondansetron.

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Sudden onset bradycardia after IV administration of Ondansetron is a possibility as observed in this case. But it can result in unstable cardiac activity going to atrial and, ventricular ectopics which may proceed to life-threatening arrhythmias. ECG monitoring and following intravenous administration protocol when the patient receives Ondansetron intravenously is advisable. We want to emphasize that Ondansetron can result in variable cardiac adverse events for which we need to be vigilant.

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