Ondansetron induced acute chorea with hyperthermia in an obstetric patient

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Objective

To describe the case of a patient who developed extrapyramidal side effects (EPSE) and hyperthermia after receiving ondansetron, a commonly used peri-operative medication.

Clinical features

32-year-old female speech pathologist of Asian descent was administered intravenous (IV) ondansetron for nausea following a difficult vaginal birth. Within one hour of receiving the ondansetron the patient developed:

- Involuntary facial movements
- Rigidity
- Aphasia
- Hyperthermia

Past medical history included:

- Polycystic ovaries

Interventions and outcomes

Three IV doses of benzatropine 0.5mg were administered to cover potential metoclopramide-induced EPSE. However, as the movements were choreiformic in nature and there was minimal response to benzatropine, metoclopramide was deemed an unlikely cause. Ondansetron was suspected as a possible contributing agent as previous cases in the literature have reported it causing acute chorea in females. Furthermore, the reaction occurred 1 hour after administration. The patient's symptoms resolved within 12 hours of the initial dose of ondansetron.

Discussion

Ondansetron is a commonly used 5-HT_3 antagonist. Severe reactions to this anti-emetic drug are rare. Differential diagnosis in this case include; serotonin syndrome and metoclopramide induced EPSE. Serotonin syndrome is characterised by locomotor signs (tremor, rigidity or clonus), autonomic instability (tachycardia, marked hyperthermia, mydriasis, diarrhoea) and altered mental status[1]. Serotonin syndrome was determined to be improbable as there was no evidence of any iatrogenic causes from the patient's history.

The hyperthermia that developed could be attributed to misoprostol use for postpartum heamorrhage, which is well documented in the literature.

The patient received metoclopramide 17 hours prior to the reaction. Metoclopramide induced EPSE often occurs within the first 24-72 hours of administration[2]. Benzatropine is effective within a few minutes of most dystonic reactions, especially those caused by metoclopramide[2]. However, in this case there was minimal effect after 3 doses of benzatropine and the reaction appeared to be more choreiformic in nature. Hence, ondansetron was believed to be the likely causative agent.

3/4/18 0215	• Presented to hospital with spontaneous rupture of membrane • Discharged with script for oral antibiotics to be taken if labour does not progress in 18 hours
2200	• Re-presented to hospital. Contractions every 3 minutes and lasting for 1 minute • Pain relief: TENS and N_2O_2
4/4/18 0045-0130	• Morphine 5mg and Metoclopramide 10mg IM • Ampicillin 1g IV
0600-0800	• Oxytocin infusion started and slowly increased to 36ml/hour • Ampicillin 1g IV given
0945- 1430	• Epidural started Rovipicaine 0.2% + Fentanyl 2microg • Oxytocin infusion slowly increased to 144ml/hr
1605-1610	• Forceps delivery due to atonic uterus • Oxytocin 10 units • Oxytocin/ergometrine 250microg IV and 250microg IM • Top-up of lignocaine 2% +adrenaline and fentanyl 50microg • Misoprostol 1g PR
1651	• Ondansetron 4mg IV
1710	• Tranexamic acid 1g IV
1750	• Patient develops: • Abnormal behaviour • Involuntary facial movements • Rigidity • Aphasia • Hyperthermia • Inability to understand verbal cues • Aphonia
1814-1845	• Three doses of benzatropine 0.5mg IV administered • Patients neurological symptoms improve slightly but do not fully resolve • Blood taken Creatinie kinase level of 321 and eGFR 42
2300-2400	• Aphonia continues • Hyperthermia resolving
5/4/18 0400	• Initial choreiformic like symptoms resolve

The neurochemical pathway of ondansetron induced EPSE is poorly understood. It is thought there may be serotonergic input to locomotor regulation in the basal ganglia and related nuclei in the limbic system[3]. The possible mechanisms of ondansetron induced nervous system effects include blockade of 5-HT receptors at central sites, blockade of cell firing and dopamine release in the nucleus accumbens[3]. One pharmacological review found that ondansetron has the ability to stop or decrease elevated mesolimbic dopamine activity and to antagonise increased locomotor activity caused by mesolimbic dopamine excess[3].

Most reported cases of ondansetron induced EPSE have occurred during treatment of nausea associated with chemotherapy, after several days of treatment and with larger doses[4]. In this case the patient developed symptoms after one dose of ondansetron. It is believed that young age and female gender may predispose patients to the risk of EPSE due to dopamine hypersensitivity from post-synaptic modifications in high oestregen states[1]. This may explain why reported cases of ondansetron induced EPSE are primarily in young women.

Conclusions

This case report highlights a rare but potentially important adverse effect of ondansetron induced EPSE. Although rare, young age and female gender may predispose patients to the risk of this reaction.

Implications for practice

$5HT_3$ antagonists are routinely used in obstetric practice, clinicians should be aware of the risk of EPSE associated with ondansetron use.

References

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