Severe Bradycardia and Hypotension Possibly Induced by Ranitidine

Nausea, vomiting, diarrhea, constipation and rash are the more frequently encountered adverse reactions of ranitidine – a selective histamine H2 receptor antagonist. Only a few cases of cardiovascular side effects have been reported [1-3].

A 10-year-old boy was admitted to our hospital for percutaneous endoscopic gastrostomy (PEG). He had had neurological disability because of neonatal bilirubin encephalopathy. He was receiving diazepam and baclofen dystonia for last six years. Laboratory examination, including whole blood count, blood chemistry results, and thyroid function tests were normal. Percutaneous endoscopic gastrostomy (PEG) tube was inserted. Ranitidine was injected at a dose of 4 mg/kg/day in four divided doses by intravenous route starting from 24 hour after the procedure. After four hours of the first dose of ranitidine, the child was noted to have bradycardia (HR 60/min) and the blood pressure fell to 80/50 mmHg 16 hours after the first dose of ranitidine. At the third day of ranitidine treatment, the heart rate was detected to be 36/min and there was common voltage drop on electrocardiography. Echocardiography was normal. Physical examination revealed no additional findings except bradycardia and hypotension. Ranitidine treatment was stopped. No treatment was given for bradycardia and hypotension because of the good general condition of the patient. Heart rate and blood pressure improved after 12 hours of discontinuation of ranitidine.

H2 receptors are reported to be present in sinus node, atrial and ventricular myocardium as well as gastric mucosa [1]. Cimetidine and ranitidine have been reported to cause significant hypotension in critically ill patients. Though gastric interventions such as PEG insertion may lead to increased vagal tone causing bradycardia, it was not seen until the first dose of ranitidine treatment in present case. Moreover, it resolved following cessation of ranitidine treatment.

Clinicians should always be aware of the possibility of rare but potentially serious cardiovascular adverse events of ranitidine, especially in sick children.

ESMA ALTINEL ACOGLU* AND SALIHA SENEL
Dr Sami Ulus Maternity and Children's Health and Diseases Training and Research Hospital, Altýndað/Ankara, Turkey
**esmaaltinel@hotmail.com*

REFERENCES

1. Vial T, Goubier C, Bergeret A, Cabrera F, Evreux JC, Descotes J. Side effects of ranitidine. Drug Saf. 1991;6:94-117.
2. Yang J, Russell DA, Bourdeau JE. Case report: ranitidine-induced bradycardia in a patient with dextrocardia. Am J Med Sci. 1996;312:133-5.
3. Smith CL, Bardgett DM, Hunter JM. Haemodynamic effects of the i.v. administration of cimetidine or ranitidine in the critically ill patient. A double-blind prospective study. Br J Anaesth. 1987;59:1397-402.
4. Genovese A, Spadaro G. Highlights in cardiovascular effects of histamine and H1-receptor antagonists. Allergy. 1997;52:67-78.

Subacute Sclerosing Panencephalitis: A Disease Not to be Forgotten

Evaluation a child with encephalitis is difficult due to the similarities in the clinical, imaging and laboratory findings of many forms of autoimmune and infectious encephalitis. Presentation of autoimmune encephalitis in childhood is often subacute, with varied clinical manifestation [1]. However, as it takes time to get the results of antibody tests for autoimmune encephalitis, immunosuppression is often started with a presumed diagnosis of AE. Due to increasing awareness of AE, many primary-care physicians are diagnosing it and starting immunomodulation, which may be detrimental at times.

In past few months, two children presented to us in vegetative state. Both children were diagnosed as AE based on their presentation with fever, behavioral changes and myoclonic jerks/focal seizures. Pulse methylprednisolone was administered to the children with presumed diagnosis of autoimmune encephalitis. There was no improvement on immunotherapy and children deteriorated to vegetative state in next 2-3 weeks. There was no history of measles in these children, and they were vaccinated (one dose of measles vaccine at 9 months). Fundus examination showed hyperemic disc, large whitish subretinal patch over posterior-pole with satellite lesions, and magnetic resonance imaging (MRI) of brain showed subtle asymmetrical hyper-intensities in peri-ventricular white-matter. Based on these findings, Subacute sclerosing panencephalitis (SSPE) was suspected, and subsequently confirmed by raised (1:625)

titers of IgG measles antibodies detected by enzyme-linked immunosorbent assay in CSF. Both children died over next one month.

In regions where SSPE is still common, we should be cautious before using immunomodulation in presumed autoimmune encephalitis. Diagnosis of SSPE is mainly based on clinical presentation, supported by elevated CSF measles antibody titers [2]. Autoimmune encephalitis clinically manifests with alteration of consciousness and/or behavioral changes, which may be associated with seizures, movement abnormalities and/or focal neurological deûcits. While in SSPE, the initial symptoms are usually subtle, include mild intellectual deterioration and behavioral changes without any apparent neurological signs; this is followed by steady motor decline and myoclonus [1-3]. However, some cases of SSPE have an acute presentation with death occurring in few weeks. Retina-, EEG- and MRI findings help to distinguish SSPE from AE. The most characteristic ophthalmic findings in SSPE are optic nerve head edema, retinal pigment epithelial changes, active or scarred chorioretinitis, and optic atrophy [4]. Periodic EEG complexes are pathognomonic features of SSPE but are not seen in all individuals [2]. In the early stages, MRI findings are normal, or cortical/subcortical asymmetrical hyperintense lesions may be observed in the posterior parts of the brain. As the disease progresses, the lesions disappear and new lesions occur symmetrically in the periventricular white-matter in association with mild cortical atrophy [2]. Apart from these findings, CSF examination for antibody provides definite diagnosis of both SSPE and AE.

To conclude, when in doubt it is better to withhold immunosuppression with methylprednisolone till we get the confirmation of a diagnosis of autoimmune encephalitis.

MAHESH KAMATE* AND MAYANK DETROJA
Department of Pediatric Neurology,
KLE University's J N Medical College,
Belgaum, Karnataka, India.
**drmaheshkamate@gmail.com*

REFERENCES

1. BrentonJ, Goodkin H. Antibody-mediated autoimmune encephalitis in childhood. Pediatr Neurol. 2016;60:13-23.
2. Gutierrez J, Issacson R, Koppel B. Subacute sclerosing panencephalitis: An update. Dev Med Child Neurol. 2010;52:901-7.
3. Graus F, Titulaer M, Balu R, Benseler S, Bien C, Cellucci T, *et al*. A clinical approach to diagnosis of autoimmune encephalitis. Lancet Neurol. 2016;15: 391-404.
4. Yuksel D, Sonmez P, Yilmaz D, Senbil N, Gurer Y. Ocular findings in subacute sclerosing panencephalitis. Ocul Immunol Inflamm. 2011;19:135-8.

Galactomannan Antigen Test for Invasive Aspergillus Infection in Febrile Neutropenic Children

Kumar, *et al.* [1] published their findings on Galactomannan antigen test for early diagnosis of invasive aspergillus infection in a recent issue of *Indian Pediatrics* [1]. The article was interesting and I seek certain clarifications:

1. What were the sites from which authors were able to isolate aspergillus for proven invasive fungal infection?
2. What were the species? Was sensitivity testing performed on all the isolates? Did authors come across any species which was resistant to voriconazole/ amphotericin B?
3. Authors mentioned that antibiotics like piperacillin-tazobactam can lead to false positive galactomannan test; it has been shown to be no longer cross-reactive [2].
4. Did some of the patients in this study have pulmonary leucostasis/hyperleukocytosis which could have led to a false impression of a fungal nodule or ground glass opacities on computed tomography.
5. Authors mentioned that they were not able to perform bronchoalveolar lavage (BAL) on patients due to thrombocytopenia; did they attempt the procedure when the platelets improved, at the end of induction therapy or on recovery from the febrile event. It is well-established that BAL galactomannan is more sensitive as well as specific for invasive fungal infections [3].

RICHA MALIK
Department of Pediatrics,
Aakash Superspeciality Hospital, New Delhi, India.
malik.richa86@gmail.com

REFERENCES

1. Kumar J, Singh A, Seth R, Xess I, Kabra SK. Galactomannan antigen test for early diagnosis of invasive