Regadenoson and seizures: A real clinical concern

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Regadenson is a commonly used vasodilator agent for resting stress-myocardial perfusion scans which was approved by this purpose by the Food and Drug Administration in April of 2008. It is an A2A adenosine receptor agonist, which compared to other nonselective vasodilators offers a rapid onset yet short duration of action, a fixed-dose bolus, and a good safety and tolerability profile particular in patients with reactive airway disease. While the initial clinical trials did not have any signals regarding increased risk of adverse effects, post-marketing surveillance has noted increased incidence of adverse events such as advanced heart block, transient QTc prolongation, and seizures (both in patients with and without prior history of seizure). This is not surprising since the clinical trials have a few thousand patients enrolled in the individual trials, while in real life practice, regadenoson is the most widely used vasodilator agent for myocardial perfusion imaging single photon emitted computerized tomography (MPI SPECT) studies, with more than 2-3 million regadenoson MPI SPECT studies performed annually in United States alone.

We recently reported the case of an elderly female who developed an episode of unresponsiveness along with advanced heart block after the administration of regadenoson.[1] While the episode of advanced heart block completely resolved after the administration of intravenous aminophylline, her altered mental status required critical care level of monitoring and serial CT scans to rule out organic pathology as the underlying etiology of the episode of unresponsiveness.

The Food and drug Administration had approved important safety label changes with the use of regadenoson in December 2009, which reflected the increased incidence of seizures noted in the post-marketing experience. While the exact risk and incidence of seizures induced by regadenoson is unknown, the Food and Drug Administration self reported database has 30 reported cases of convulsions.[2] Although the exact mechanism responsible for the causation of seizures associated with the use of regadenoson is not yet clear, it has been suggested that the A2A receptors located at various location in the central nervous system, including the striatum, nucleus accumbens, tuberculum olfactorium, cortex, and hippocampus, may have a role in initiation of seizures.[3] It must be noted that these A2A receptors are the same subgroup of receptors where regadenoson acts and produces coronary vasodilation. In the central nervous system, these A2A receptors have both inhibitory and excitatory effects, and in the setting of an appropriate substrate can potentially lower seizure threshold by increasing glutaminergic excitotoxicity. This role of the A2A receptors has been demonstrated in animal models.[4]

Astellas had updated the regadenoson package insert in July 2014 to reflect that regadenoson may lower seizure threshold and aminophylline should not be used in cases of seizures associated with regadenoson.[5] These seizures may be of new onset, or may be recurrences. In addition it provides warning that some seizures are prolonged and may require urgent anticonvulsive

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management. In addition, it is recommended that during the initial triaging of patients, patients should be asked about history of seizures.

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