The Blue Pacific Ocean

DUQUESNE UNIVERSITY
MYLAN SCHOOL OF PHARMACY

PIC QUESTION OF THE WEEK: 11/16/09

Q: Are there any reports of the serotonin syndrome attributed to the use of methylene blue?

A: Methylene blue is a thiazine dye administered intravenously for the treatment of drug-induced methemoglobinemia. It has also been used as an intraoperative dye marker, especially in patients undergoing parathyroidectomy. The drug continues to be available in a few oral combination products used for the treatment of cystitis. Serotonin syndrome is typically described as a combination of symptoms including mental status changes, neuromuscular toxicity, and autonomic dysfunction due to excess serotonergic activity. It is often related to the use of a combination of serotonergic compounds, e.g. selective serotonin reuptake inhibitors (SSRIs), monoamine oxidase inhibitors, meperidine, *triptan* medications, lithium, amphetamines, etc. Some initial reports of serotonin syndrome due to methylene blue toxicity occurred earlier this decade and additional cases continue to be documented. In all cases, the drug was being used as parathyroid marker and administered prior to surgery as an intravenous infusion over a period of approximately 1-2 hours. The dosage of methylene blue in these patients ranged from 1.75-7.5 mg/kg. Symptoms of serotonin syndrome usually begin in the immediate postoperative period and during admission to the post-anesthesia care unit (PACU). Most patients were subsequently admitted to intensive care units and required tracheal intubation and ventilatory support. Each of these patients had been prescribed an SSRI, serotonin norepinephrine reuptake inhibitor (SNRI), or clomipramine (a potent serotonergic tricyclic antidepressant). No cases have been reported in patients only receiving methylene blue. Likewise, oral agents containing the dye have not been implicated in cases of serotonin syndrome. It is now established that methylene blue inhibits monoamine oxidase A (MAO A) resulting in accumulation of excessive amounts of serotonin and its associated toxicities. Several authors consider this to be a predictable consequence of the combined administration of SSRIs and methylene blue and prefer the term *serotonin toxicity* rather than serotonin syndrome. Because of the long half-life of many SSRIs, discontinuing their use for a few days prior to parathyroidectomy may be insufficient to prevent toxicity upon injection of methylene blue. Alternative methods for identifying the parathyroid gland should be considered in all patients receiving SSRIs who are about to undergo a parathyroidectomy.

References:

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