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PALLIATIVE CARE CASE OF THE MONTH

Transdermal Granisetron for Refractory Nausea and Vomiting

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Case: Ms JB is a 32 year old woman with type 1 diabetes who underwent a living related donor renal transplant and a subsequent pancreas transplant. Unfortunately, both transplants were complicated by rejection and graft failure requiring re-initiation of hemodialysis in 2007. Since that time she has suffered with constant, intractable nausea with multiple episodes of vomiting throughout each day. Her symptoms were initially thought related to diabetic gastroparesis but they did not respond to metoclopramide, erythromycin or pylorus muscle botulinum toxin injections. An electrical gastric stimulator was to be placed but was aborted when a gastric emptying study was normal. Extensive workup, including laboratory studies, endoscopy, CNS imaging and abdominal imaging, was unrevealing. She received little or no benefit from adequate trials of domperidone, prochlorperazine, ondansetron, oral granisetron, promethazine, trimethobenzamide, scopolamine, mirtazapine, dronabinol, pancreatic enzymes and a proton pump inhibitor.

She underwent voluntary admission to a psychiatric hospital for treatment of any possible contributing eating disorder without any improvement. Since 2007, she has had more than 40 admissions to the hospital for nausea and vomiting. A feeding J-tube was placed to maintain adequate nutrition in 2008. She presented to the Palliative Care clinic in 2010 for further management of her nausea and vomiting. After a complete history and physical, the etiology of her symptoms remained somewhat elusive. She had nausea before her transplant and it had resolved when the kidney was working then recurred when it failed so the final conclusion was that her symptoms may be due to a poorly defined metabolic process related to her renal failure. Olanzapine was initiated on the first visit for refractory nausea and vomiting and the patient was referred to psychology and psychiatry to help with coping and to address underlying depression and anxiety. At the subsequent visit she noted some benefit so the olanzapine dose was increased and a granisetron transdermal patch was added. At the next visit her symptoms had improved dramatically with a clear temporal relation to starting the granisetron patch. She was only vomiting once or twice in the morning and was relatively asymptomatic through the day. In her first clinic visit she had vomited multiple times through the visit and appeared miserable.

At this visit she was asymptomatic, neatly dressed, wearing makeup and was thrilled at this new level of symptom control which was allowing her to re-engage her life.

Discussion: There were many factors that likely contributed to the dramatic improvement in Ms JB's refractory nausea and vomiting. Better psychiatric care through the palliative care psychologist and psychiatrist almost certainly played a role in her overall clinical turn-around. The close attention, serial visits and supportive counseling she received in the Palliative Care clinic could also have been therapeutic. Uptitration of her olanzapine also likely was helpful. Olanzapine is an atypical antipsychotic that works on multiple receptors including dopaminergic, serotonergic, adrenergic, histaminergic and muscarinic receptors. Of particular interest is its antagonism of 5HT2 receptors which are located in the vomiting center and are not well targeted by other traditional antiemetics. Multiple small trials have demonstrated efficacy of olanzapine for chemotherapy-induced nausea and vomiting.[1] Many palliative care practitioners are now also starting to use olanzapine for refractory nausea and vomiting in patients with advanced cancer and other life-limiting conditions.[2-4]

Even with all of these possible contributors to her improvement, there still seemed to be a clear benefit that came with initiation of the granisetron patch. While intravenous and oral granisetron have been available for some time, transdermal granisetron (Sancuso©) is a relatively new addition to the practitioner's toolbox for difficult to control nausea and vomiting. Transdermal granisetron was approved by the FDA for chemotherapy-induced nausea and vomiting (CINV) in September of 2008 based largely on a trial of 582 patients receiving multi-day moderately or highly emetogenic chemotherapy. Patients received either oral or transdermal granisetron and achieved equally good control of their symptoms with either method (approximately 60% in each group achieving complete symptom control). The most common side effect in both groups was constipation.[5] The patch is an 8x6cm clear, plastic-backed patch and is worn for 7 days. Pharmacokinectic studies suggest that the patch delivers a dose equivalent to 2 mg of oral granisetron each day it is worn.[6]

It is thought to exert its antiemetic effect through antagonism of 5HT3 receptors in the gut and chemoreceptor trigger zone.[7] Experience with the patch outside of CINV, however, is limited. This case suggests that transdermal granisetron may have a role in other cases of refractory nausea and vomiting. It is unclear why the transdermal form of the drug worked so much better than the oral version for Ms JB. It could reflect absorption issues, especially if she was unable to keep the pills down. It could also reflect compliance issues and may bring into question the adequacy of her prior trial of oral granisetron. Whatever the mechanism, however, the result was dramatic. Further study of this agent in settings other than CINV is clearly needed. Hopefully these results can be replicated and other patients with difficult-to-control nausea and vomiting can achieve life-changing results similar to those achieved by Ms. JB.

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