



**Gabapentin for Refractory Chemotherapy-Induced Nausea and Vomiting
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Case: Palliative Care was consulted on Ms. B, a 43 year old woman with stage III peripheral T cell lymphoma who is undergoing chemotherapy with A-DHAP (alemtuzumab with dexamethasone, cisplatin and cytarabine). Each cycle has been associated with difficult to control nausea and vomiting and a gradually increasing stocking-glove neuropathy. With prior cycles, the symptoms would resolve and she would have a couple of good weeks before the next cycle was due to begin. With the most recent cycle, however, the symptoms were worse and never fully resolved. She was admitted for cycle #4 of therapy and, despite appropriate antiemetics, her nausea and vomiting became severe. Her peripheral neuropathy also worsened and palliative care was consulted for help with symptom control. The palliative care consultant found no cause for her symptoms other than chemotherapy based on a thorough history and physical as well as a brain MRI, CT of the abdomen and pelvis, flat plate of the abdomen and laboratory testing including electrolytes, liver function tests, and a cortisol level. The nausea did not appear anticipatory and did not respond significantly to lorazepam. Haloperidol and prochlorperazine caused agitation and metoclopramide and steroids caused hypertension. She got no benefit from ondansetron, scopolamine or dronabinol. She got a small benefit with granisetron and then some more benefit with mirtazapine although the symptoms remained very bothersome. Eventually she was started on 300mg of gabapentin at night for her neuropathy and the next day her pain was slightly improved but, remarkably, her nausea had resolved. She stayed in the hospital for 2 more days and had no recurrence of nausea or vomiting.

Discussion: There are many potential explanations for the resolution of Ms B's chemotherapy-induced nausea and vomiting (CINV). It is possible that her nausea simply resolved with time but this seems unlikely since her symptoms lasted much longer with prior cycles. The gabapentin could have served as an opioid-sparing agent that resulted in improved nausea because the patient was taking fewer doses of oxycodone. The patient did decrease her use of oxycodone from 3 tabs in 24 hours to 2 tabs but she saw no temporal relation of the symptoms to opioids and continued to take 2-3 tabs per day in the subsequent days with no return of her nausea.

Pain itself can also be emetogenic but it seems unlikely that such a low dose of gabapentin would have such a profound effect and, although the patient did believe the pain was improved, it was certainly still present.

A final explanation may be that gabapentin has intrinsic antiemetic effects and a small body of literature is developing to support this hypothesis. Interest in the use of gabapentin for this indication began when clinicians at the University of Rochester initiated gabapentin for hot flushes in a patient with breast cancer and noted resolution of her refractory nausea.¹ They subsequently performed an open-label trial of gabapentin 300-600mg by mouth three times daily in 9 breast cancer patients receiving doxorubicin and cyclophosphamide.¹ All patients also received standard antiemetics before and after chemotherapy, including ondansetron, dexamethasone, lorazepam and prochlorperazine. Subjects received gabapentin for cycles 2 and 4 but not 1 and 3. Gabapentin was associated with a median reduction of 3 points on an 8 point scale for acute and delayed CINV with three of the patients reporting complete resolution of their symptoms. Another small noncontrolled trial also showed a possible benefit in 24 patients with a history of difficult to control CINV receiving a variety of chemotherapy regimens.² Patients were treated with a 5HT₃ antagonist, dexamethasone and gabapentin started at 300mg daily two days before chemotherapy then twice daily the day before chemotherapy then three times daily for the following five days. 75% of these patients who had significant CINV with prior cycles had no or mild nausea on the day of chemotherapy and 79-92% had no or mild nausea on each of the remaining 5 days. Similarly 58% had no vomiting on the day of chemotherapy and 75-92% had no vomiting on each of the remaining 5 days. A larger body of literature³⁻⁶ is also developing showing a possible benefit of gabapentin in reduction of postoperative nausea and vomiting (PONV), including two recent double-blind, randomized, placebo-controlled trials with a combined recruitment of 215 patients undergoing cholecystectomy that showed a 37-44% reduction in PONV.^{5,6}

For palliative care consultations please contact the Palliative Care Program at PUH/MUH, 647-7243, beeper 8511, Shadyside Dept. of Medical Ethics and Palliative Care, beeper 412-647-7243 pager # 8513 or call 412-623-3008, Perioperative/ Trauma Pain 647-7243, beeper 7246, UPCI Cancer Pain Service, beeper 644-1724, Interventional Pain 784-4000, Magee Women's Hospital, beeper 412-647-7243 pager #: 8510, VA Palliative Care Program, 688-6178, beeper 296. Hillman Outpatient: 412-692-4724. For ethics consultations at UPMC Presbyterian-Montefiore, and Children's page 958-3844. With comments about "Case of the Month" call David Barnard at 647-5701.



The exact mechanism by which gabapentin might exert an antiemetic effect is unclear but it has been postulated that tachykinins may play a role. Gabapentin is thought to mitigate tachykinin neurotransmitter activity and, in animal models, tachykinins have been implicated in the pathogenesis of CINV with tachykinin receptor antagonists producing reduced acute and delayed emesis.¹

While further research is clearly needed, the case of Ms B and the early data cited above suggest that gabapentin may have a role as an antiemetic for refractory CINV and PONV. Furthermore, since it seems to exert this effect at relatively low doses, it is likely to be well tolerated by most patients. This small evidence of benefit and low risk of side effects makes gabapentin an attractive potential addition to the clinician's toolbox for addressing the intense suffering of patients with intractable nausea and vomiting.

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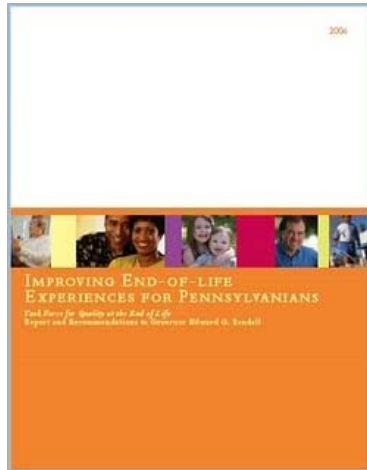
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PA House of Representatives Holds Hearing on 2007 End-of-Life Care Report

The PA House of Representatives Committee on Aging held a hearing on November 18, 2009 about the State Task Force's End-of-Life Care report, *Improving End-of-Life Experiences for Pennsylvanians*. This report was co-authored by several members of the Institute and CQEL. John Michael Hall, Secretary of Pennsylvania Department of Aging, and Ann Torregrossa, Director of the Governor's Office of Health Care Reform, gave testimony regarding the state of end-of-life care in Pennsylvania. The hearing covered the need to address barriers to accessing palliative care. These barriers include lack of awareness and education about end-of-life care among members of the public and health professionals and



insufficient or limited health insurance coverage outside of hospice coverage.

Improving End-of-Life Experiences for Pennsylvanians.
Task Force for Quality at the End of Life.

The transcript from the November 18th hearing is available on the Pennsylvania House of Representatives website: http://www.legis.state.pa.us/cfdocs/legis/tr/transcripts/2009_0200T.pdf.

Dr. Susan Hunt to Present at Dying Workshop March 2010

The Institute's Dr. Susan Hunt will be a guest speaker at a local workshop titled, Being with Death and Dying. The workshop is suited for medical professionals working with dying and illness, those who are ill, and those who would like to look deeply into the meaning of death and dying within the framework of a spiritual path. The workshop faculty will teach practices to support the dying and present compassionate care from a spiritual perspective. For more information or to register, please visit: <http://www.olmoling.org/>

The Institute Welcomes Visiting Palliative Care Physician

Dr. Ioseb Abesadze, Chief of the Palliative Care Institute of the Republic of Georgia, in Tbilisi, and Medical Director of the Palliative Care Unit of Cancer Prevention, recently visited Pittsburgh and the Institute to Enhance Palliative Care on January 8-14, 2010. Palliative care is a very young discipline in Georgia, as it is in



Institute Director, Dr. David Barnard with Governing Council Member and Honorary Consul General to the Republic of Georgia, Mahnaz Harrison with Visiting Palliative Care Physician from Georgia, Ioseb Abesadze.

most of the East European states of the former Soviet Union with Dr. Abesadze being a leader in the effort to enlarge and improve palliative care in his country. He has participated in international educational programs at San Diego Hospice where he will return after visiting the Institute. During his visit Dr. Abesadze learned clinical, administrative, and educational aspects of our program and those of palliative care in our region. He met with members of the Institute, as well as the Coalition for Quality at the End of Life to discuss the state of palliative care in Georgia as well as the roles both organizations play in improving palliative care in our region. He spent time at UPMC and Family Hospice and Palliative Care to learn about palliative care delivery in these institutions.

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