CASE REPORT

Treatment of Medication Intolerance with Lactase in a Complex Palliative Care Patient

REGIS VAILLANCOURT, RABIAH SIDIQUI, CHRIS VADEBONCOEUR, MARION RATTRAY, and DORIS LARIVIÈRE,
Roger's House Pediatric Palliative Hospice, Ottawa, Ontario, Canada

INTRODUCTION

Lactose intolerance is a clinical deficiency of the intestinal enzyme lactase, which is responsible for hydrolyzing the milk sugar lactose into glucose and galactose for absorption. Such a deficiency results in abdominal pain, distention, borborygmi, flatulence, diarrhea, or, occasionally, systemic symptoms such as muscle and joint pain, fatigue, eczema, and mouth ulcers upon ingestion of disaccharide (1). In children, symptoms can become severe and prolonged, and may also be associated with complications such as bacterial proliferation, dehydration, and metabolic acidosis. Infants with galactosemia, a condition in which galactose cannot be converted to the metabolically useful sugar glucose, experience similar illness with lactose ingestion (2). Lactose intolerance affects 33 to 50 percent of the world’s population and becomes increasingly common with age, as most mammals lose 70 to 90 percent of their lactase enzyme within a few years of weaning (3, 4). Lactase deficiency varies widely with race: African American, Native American, Middle Eastern, and Asian populations have the highest incidence (60 to 90 percent), whereas only 10 percent of Scandinavian or European descendents are affected (5). While there is patient variation in tolerance, the majority experience gastrointestinal symptoms after the ingestion of approximately 10 g of lactose, equivalent to one glass of milk (5). Currently, diagnostic tests employ loads of 50 to 100 g of lactose, but the use of such high quantities has been questioned since sensitivity to lactose levels of 3 g or less has been demonstrated (5, 6). In fact, the modest presence of lactose as a bulking agent in pharmaceutical products has been the source of medication intolerance in several instances. We report the case of a complex pediatric patient who experienced such a reaction, and in whom treatment with exogenous lactase provided significant relief.

CASE REPORT

C.H., a three-and-a-half-year-old Caucasian boy, was admitted for a routine respite stay at a pediatric palliative care hospice in the fall of 2006. C.H. was born with complex congenital anomalies including pontine dysplasia, optic pituitary dysplasia, central diabetes insipidus, adrenal insufficiency, hypothyroidism, epilepsy, and gastric dumping syndrome associated with hypoglycemia. In 2004, a fundoplication procedure had been performed to manage his severe gastroesophageal reflux disease. Although there was no prior history of lactose intolerance, he was on an enteral lactose-free feed with a strict volume intake of 1,845 ml daily. In the summer of 2006, a dietary switch from the formula Peptamen Jr. (Nestlé Inc.) to Nutren Jr. (Nestlé Inc.) was concurrent with resolution of his dumping syndrome and hypoglycemia, as well as his seizures. Although these symptoms had resolved, C.H. continued to suffer from gastrointestinal discomfort and intense pain, manifested as sporadic screaming episodes and abdominal distention.

C.H. communicated only via touch, since he could not see, hear or speak. C.H.’s mother described his symptoms as “neurological screeching;” his bloating was so intense that venting of his gastric tube using a syringe yielded 1,000 ml of gas at a time. C.H. was on a complex medication regimen that included desmopressin (Ferring Pharmaceuticals, 0.025 mg p.o bid, 0.05 mg p.o qhs), clonidine (Novopharm Ltd., 0.05 mg p.o qhs), hydrocortisone (Pfizer Inc., 3.5 mg p.o bid), clobazam (Novopharm Inc., 5 mg p.o daily), levothyroxine (Abbott Laboratories., 0.025 mg p.o daily), omeprazole (AstraZeneca Inc., 10 mg p.o bid), metronidazole (Apotex Inc., 180 mg p.o bid), morphine hydrochloride (ICN Pharmaceuticals. 1 mg p.o. q3h prn) and Microlax enemas (Pharmacia Inc., prn). Small bowel bacterial overgrowth was the working diagnosis for his gastrointestinal symptoms, and a formulation of L. acidophilus & L. casei (Bio-K+ International Inc., 30 ml p.o qid)
was given in addition to the metronidazole for this purpose. C.H.’s mother and the palliative care team finally resorted to morphine to alleviate his pain (1 mg three to four times daily), which calmed him down and induced sleep, but did not manage the gas and pain.

In September 2006, the pharmacist suspected lactose intolerance after discerning the number of tablets containing lactose as a binding agent, as per their drug monographs in the Compendium of Pharmaceuticals and Specialties (CPS) (7). Exogenous β-galactosidase with 3000 units of lactase activity (known under the generic name of lactase, Life Brand, 3000 Units) was initiated with C.H.’s medications and feeds, and he improved drastically. His screaming abated, his abdominal swelling decreased, and he was able to discontinue the morphine within three weeks. Metronidazole was also removed from his regimen within one month. C.H.’s abdominal girth also improved over subsequent weeks; according to his mother he eventually decreased by two pant sizes. Most notably, C.H. began to grow. For a full year prior to starting the lactase supplements he weighed 11 kg; within nine months after the lactase, he gained more than three kilograms. C.H. has since remained a more content boy, and the effect on his family has been equally positive.

DISCUSSION

Lactase deficiency varies widely in severity but the majority of patients can tolerate a dose of 12 to 18 g of lactose (8). Certain patients, however, have been noted to experience gastrointestinal symptoms after exposure to much lower quantities (6), and there appears to be no minimal threshold of lactose consumption required for inducing sensitivity. There have been documented cases of lactose intolerant individuals experiencing adverse reactions to the lactose filler in their medications (9-17). In one report, the onset of diarrhea, borborygmi, flatulence, and abdominal discomfort followed the ingestion of flutamide capsules, which contain at least 210 mg of lactose each (11). In another case, inhalation of cromolyn sodium capsules containing only 20 mg of lactose each induced similar symptoms (10). It should be noted that up to 80 percent of the cromolyn dose inhaled from a turbuhaler can be swallowed, indicating that the patient reacted to an exposure of less than 16 mg of lactose.

Among the 10 medications that C.H. was taking, five contained lactose. The quantity of lactose in each of those medications is outlined in Table 1. C.H. had a total intake of approximately 360 mg of lactose per day. Consistent with previous case reports, this quantity is sufficient to induce medication intolerance in a highly sensitive lactase-deficient patient.

Symptoms of lactose intolerance occur when undigested lactose reaches the large intestine, osmotically draws in fluid, and is fermented by colonic bacteria (12). The precise pathogenesis of C.H.’s symptoms may not be entirely explained by this mechanism, since the quantity of lactose he consumed was so small relative to the symptoms he experienced. Petri et al. have proposed a mucosal hyperreactivity, perhaps immune-mediated etiology for this type of reaction (9). It is clear, however, that lactase deficiency was the source of C.H.’s medication intolerance. A temporal relationship between lactase supplementation and clinical improvement supports this finding. Following the administration of lactase, three significant changes occurred: (1) the resolution of C.H.’s screaming and a drastic reduction in gastrointestinal distention, (2) the successful discontinuation of gastrointestinal and pain medications, and (3) an increased rate of weight gain. Although no hydrogen breath test or intestinal biopsy was performed to definitively diagnose lactose intolerance, C.H.’s case provides indirect but strong evidence that medication intolerance can occur due to the presence of lactose therein.

### Table 1 / Lactose content of C.H.’s medications

<table>
<thead>
<tr>
<th>Medication</th>
<th>Quantity of lactose per tablet (mg/tab)*</th>
<th>Daily dose (no. of tablets/day)</th>
<th>Daily lactose ingestion (mg/day)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DDAVP</td>
<td>unavailableb</td>
<td>1.0</td>
<td>unavailable</td>
</tr>
<tr>
<td>Novo-clonidine</td>
<td>89.0</td>
<td>0.5</td>
<td>44.5</td>
</tr>
<tr>
<td>Novo-clobazam</td>
<td>80.0</td>
<td>0.5</td>
<td>40.0</td>
</tr>
<tr>
<td>Synthroid</td>
<td>62.8</td>
<td>1.0</td>
<td>62.8</td>
</tr>
<tr>
<td>Cortef</td>
<td>300.0</td>
<td>0.7</td>
<td>210.0</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td></td>
<td>&gt;357.3 mg/day</td>
</tr>
</tbody>
</table>

*Obtained from contacting respective manufacturers
bNot disclosed by manufacturer
CONCLUSION
After months of discomfort, treatment with exogenous lactase supplements alleviated the distress and pain in a complex palliative care patient. Many drug formulations contain lactose, owing to its useful physical and chemical properties as a diluent or filler in solid oral dosage forms. In the CPS alone, 795 drug monographs list lactose as a non-medicinal ingredient (a quick reference list can be found in the lilac pages of the CPS) (7). The lactose base in medications may cause a range of gastrointestinal symptoms, especially in sensitive lactose intolerant patients. Those who experience such symptoms should be evaluated for lactase deficiency and have their medications reconsidered, or receive appropriate treatment. Health care professionals should be aware of the potential harm that lactose fillers can cause, and lactose-free alternatives should be sought when possible.

Testimonial
"When the palliative team first approached us and suggested giving our son a lactase supplement with his meds we were very skeptical. With the amount of pain that our son suffered, including frequent hospitalizations due to feeding issues, it was difficult for us to understand that Lactaid could make such a difference. But when we did start it, it was not long before we saw a difference. He became a much happier little boy, caring for him was easier, the level of pain decreased, his abdomen decreased in size, hospitalizations decreased and he started growing developmentally. Sometimes the simpler things must be considered even in complex patients, and they can have a huge impact. Lactaid has changed our life."

– C.H.'s mother

Date received, August 22, 2008; date accepted, January 12, 2009.

REFERENCES
The following is an alphabetical list of people who contributed to this issue of the Journal of Palliative Care. Affiliations and addresses, which were current at press time, may have since changed.

**Arup, Katherine, PhD**
School of Canadian Studies
Carleton University
1125 Colonel By Drive
Ottawa, Ontario, Canada K1S 5B6

**Barnes, Peter, M Div, D Min**
Assistant Professor
Faculty of Human Sciences,
Counseling and Spirituality
Saint Paul University
223 Main Street
Ottawa ON, Canada K1S 1C4

**Brajtman, Susan, RN, PhD**
Associate Professor, School of Nursing
University of Ottawa, 451 Smyth Road
Ottawa, Ontario, Canada K1H 8M5

**Bridge, Douglas T, BMedSc, MBBS, FRACP, FRCP**, **FACPM, DTM & H**
Palliative Care Service, Royal Perth
Hospital, Department of Medicine
University of Western Australia
Wellington Street Campus, Box X2213
Perth, West Australia 6847

**Brown, Barbara, BSN, MSN, EdD (c)**
208-60 Cardigan Street
Guelph, Ontario, Canada N1H 3Z6

**Bucelin, Thierry, MD**
Clinical Pharmacology Division
Department of Medicine
Centre hospitalier universitaire Vaudois
Avenue Pierre Decker 11
1011 Lausanne, Switzerland

**Butew, Stephen, MA, PhD**
Associate Professor and Director of Research,
Department of General Practice and Primary Health Care
University of Auckland
Private bag 92019
Auckland, New Zealand

**Cantin, Boris, MD**
Palliative Care Service
Department of Medicine
Centre hospitalier universitaire Vaudois
Avenue Pierre Decker 11
1011 Lausanne, Switzerland

**Chan, Lisa, RN, PhD (c)**
School of Nursing, McGill University
Wilson Hall, 3506 University Street
Montreal, Quebec, Canada H3A 2A7

**Cohen, Robin S, PhD**
Project Director, Lady Davis
Institute for Medical Research
Research Director & Associate Professor
Division of Palliative Care
Departments of Medicine and Oncology
Faculty of Medicine, McGill University
McIntyre Medical Building
3655 Promenade Sir William Osler
Montreal, Quebec, Canada H3G 1Y6

**Condon, Sean, MD**
Research Investigator
Bastyr University Research Center
1450 Juanita Drive NE
Kensmore, Washington, USA 98028

**Diehn, Paula, PhD**
Professor, Department of Health Services and Department of Biostatistics
School of Public Health and Community Medicine
University of Washington, Box 357232
Seattle, Washington, USA 98195

**Downey, Lois, MA**
Research Consultant, Division of Pulmonary and Critical Care Medicine
School of Medicine
University of Washington
Harborview Medical Center
Box 399765, 325 Ninth Avenue
Seattle, Washington, USA 98104

**Fisher, Douglass, MA**
Program Manager, Fred Hutchinson Cancer Research Center
1100 Fairview Avenue N
Seattle, Washington, USA 98109

**Hall, Elizabeth**
1 Iremong Road
Colchester, Essex, UK CO3 3AT

**Hall, Pippa, MD, CCP, MFA, FCP**
Associate Professor
Department of Family Medicine
Faculty of Medicine
University of Ottawa
Program Director, Palliative Medicine Residency Program
SCO Health Service
43 Bryn Street, Ottawa
Ontario, Canada K1N 5C8

**Harris, Janet, MSW, PhD**
Centre for Evidence Based Practice
Bergen University College
PO 7030, 5020 Bergen, Norway

**Kap, Caprice, PhD**
Assistant Research Scientist
Departments of Epidemiology
Health Policy Research
Institute for Child Health Policy
University of Florida
1329 SW 16th Street, Rm 5130
Gainesville, Florida, USA 32610

**Kozak, Leila, PhD**
Postdoctoral Fellow, Northwest Health Services, Research & Development
Service Center of Excellence
Veterans Affairs Puget Sound Health Care System
Metropolitan Park West, suite 1400
1100 Olive Way, Seattle
Washington, USA 98101

**Lafferty, William E, MD**
Professor and Hicklin Endowed Chair
Office of Health Services and Public Health Outcomes Research
Department of Informatics
School of Medicine
University of Missouri (Kansas City)
2301 Holmes Street
Kansas City, Missouri, USA 64108

**Lai, Ming-Liang, MD**
Professor, Department of Neurology
Medical College
National Cheng-Kung University
Tainan, Taiwan

**Lawrèvre, Doris**
Roger's House Pediatric Palliative Hospice
390 Smyth Road, Ottawa
Ontario, Canada K1H 8L2

**Macdonald, Mary Ellen, PhD**
Assistant Professor, Departments of Pediatrics and Oncology
School of Nursing, McGill University
Wilson Hall, 3506 University Street
Montreal, Quebec, Canada H3A 2A7

**MacLean, Alex, MD, BSc(C)**
PGY 2 Internal Medicine
Queen Elizabeth II Health Sciences Centre
Dalhousie University
1351 Dresden Row #302
Halifax, Nova Scotia, Canada B3J 2J9

**Madden, Vanessa, BSc**
Research Coordinator
Departments of Epidemiology and Health Policy Research
Institute for Child Health Policy
University of Florida
1329 SW 16th Street, Rm 5130
Gainesville, Florida, USA 32610

**Marston, Joan, BSc(C)**
National Pediatric Manager
Hospice Palliative Care Association of South Africa
PO Box 38795
Pinelands 7430 South Africa

**Mazzocato, Claudia, MD**
Palliative Care Service
Department of Medicine
Centre hospitalier universitaire Vaudois
Avenue Pierre Decker 11
1011 Lausanne, Switzerland

**McAllum, Carol, RN, DNP**
Palliative Care Physician
Hawke's Bay Hospital
Omanu Road
Hastings, New Zealand
N.B.  Note Well

Conferences

July 19-22, 2009 – The 5th International Aids Society Conference on HIV Pathogenesis, Treatment and Prevention is being held at the International Convention Centre in Cape Town, South Africa. www.ais2009.org

September 10-11, 2009 – Multiculturalism, Religions and Bioethics is the theme of the European Association of Centres of Medical Ethics annual conference, being held in Venice, Italy, co-hosted by the University of Venice and Fondazione Lanza in Padua. http://www.webethics.net/eacme2009/


October 18-21, 2009 – Voyages in Care and Understanding is the theme of The Canadian Hospice Palliative Care Association conference being held at the Winnipeg Convention Centre, Winnipeg, Manitoba, Canada. http://conference.chpca.net/ For information contact the national conference coordinator Michael Peterson at 1-800-668-2785 ext.225 or mpeterson@bruyere.org

October 28-29, 2009 – The Space Between 2 is the name of the 2nd palliative care conference organized by Highland Hospice being held at Drumossie Hotel, Inverness, Scotland. For more information visit www.highlandhospice.org or call 01463 243132.

November 24-26, 2009 – Making Life before Death Matter is the theme of the Help the Hospices Conference being held at the Harrogate International Conference Centre, Harrogate, England. www.helptehospices.org.uk/2009conference/ For more information, call Saima Masters 020 7520 2911 or write to conference@helptehospices.org.uk