Objectives: To describe patterns of and factors associated with antiemetic use among a population-based sample of children with acute gastroenteritis; to determine if filling a prescription for an antiemetic is associated with a significant risk of adverse events; and to determine if filling a prescription for an antiemetic is associated with an increased risk of subsequent health care use.

Method and Design: Retrospective cohort study of 20222 children aged 1 month to 18 years, receiving Medicaid, who had a first diagnosis of gastroenteritis, diarrhea, or vomiting between January 1, 1998, and December 31, 1998.

Main Outcome Measures: Presence of a claim for an antiemetic in the 3 days after the initial diagnosis of acute gastroenteritis, subsequent health care usage, and an adverse event within 14 days of the initial diagnosis.

Results: Parents of 1802 children (8.9%) with acute gastroenteritis had a prescription for an antiemetic filled within 3 days of the index visit. Factors associated with antiemetic prescription filling for children include older age, provider type (emergency physician, family physician, or general practitioner vs pediatrician), Spanish as the primary language, and rural residency. There was no difference in adverse events between children for whom an antiemetic prescription was filled and for those who did not have an antiemetic prescription filled (odds ratio, 0.68; 95% confidence interval, 0.31-1.46). No difference in risk of subsequent health care use was seen in children who had an antiemetic prescription filled and those who did not (incidence rate ratio, 1.04; 95% confidence interval, 0.94-1.16).

Conclusion: Antiemetic use among children with acute gastroenteritis is common and adverse effects seem to be rare.

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CUTe gastroenteritis (AGE) is a common cause of physician visits and hospitalizations in young children. Children younger than 5 years average 1 to 2 episodes of diarrhea per year.1 In the United States, AGE accounts for 2.1 to 3.7 million physician visits, about 20% of all outpatient visits for children younger than 5 years,1,2 and 220000 hospitalizations a year.1,3 In addition, it is estimated that the national health care costs for diarrhea-associated disease in children younger than 5 years is $411 million a year.4

The pharmacologic treatment of AGE, with either over-the-counter or prescription medications, is common in adults.5 In 1996, the American Academy of Pediatrics (AAP) published a practice guideline on the outpatient treatment of children between 1 month and 5 years of age.5 Antiemetics were not routinely recommended because of lack of evidence of benefit and concern for potential adverse effects.5 However, some physicians continue to prescribe antiemetics for treatment of AGE in children despite the lack of evidence of their efficacy and safety, perhaps in response to parental pressure or anecdotal evidence of their efficacy. Data on current usage patterns of antiemetics are lacking.

The primary objectives of this study were (1) to determine, at a population level, the proportion of children for whom a prescription for antiemetics for the treatment of AGE was filled and (2) to determine factors associated with the prescription filling of these medications. The secondary objectives of this study were (1) to determine if children for whom a prescription for antiemetics was filled were more likely to have adverse events (allergy, adverse drug effect, or extrapyramidal reaction) and (2) to determine if children for whom a prescription for antiemetics was filled had an increased risk of subsequent health care use.
This was a retrospective cohort study using Washington State Medicaid claims and encounter data.

PATIENTS

The study population consisted of children who were enrolled in Washington State’s Medicaid program during 1998. Inclusion criteria were (1) children aged between 1 month and 18 years who had a first diagnosis of AGE, diarrhea, or vomiting in the 1998 calendar year in the first 3 available International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9 CM) diagnostic codes and (2) continuous Medicaid enrollment for at least 3 months (including 1 month prior to and 1 month after the index visit).

DIAGNOSES AND MEDICATIONS

The ICD-9 CM codes were used to identify visits for AGE, diarrhea, or vomiting. Acute gastroenteritis from viral, bacterial, and parasitic causes were included as were nonspecific diarrhea and nausea, vomiting, or both. (A complete list of ICD-9 CM codes is available from us on request.) An antiemetic was considered to be prescribed to treat AGE if dispensed within 3 days of the index diagnosis of AGE.

A list of antiemetics was compiled using National Drug Codes. Adverse events were defined using ICD-9 CM codes for adverse drug effects, allergic reactions, or extrapyramidal reactions since these are the most commonly described reactions noted in the literature. (A complete list of ICD-9 CM codes for these events is available from us.)

The patient demographic variables included age, sex, primary language spoken, and urban or rural residency. Residence referred to the place of residence during the visit, with urban and rural defined by the rural-urban commuting area codes. The rural-urban commuting area codes, developed by the Federal Office of Rural Health Policy, US Department of Agriculture, and the University of Washington, Seattle, combine information on commuting data and US Census Bureau definitions of urbanized areas to classify ZIP code areas as urban or rural at the subcounty level. Institutional review board approval was obtained by the Washington Department of Social and Health Services, Olympia, and the University of Washington.

STATISTICAL ANALYSIS

The sample was divided into those patients who had an antiemetic prescription filled within 3 days of the index visit and those who did not. Univariate descriptive statistics were compared between these 2 groups using unpaired, 2-sample, t or χ² tests, as appropriate. Multivariable logistic regression was used to model predictors for having an antiemetic prescription filled. In analyzing adverse events, children for whom antiemetic prescriptions had been filled within 3 days of diagnosis were compared with children for whom no antiemetic prescription was filled. Few children had more than 1 antiemetic prescription filled within 3 days of diagnosis to treat AGE if dispensed within 3 days of the index visit. This analysis focused on children who filled an antiemetic prescription on the day of the index visit (74.7% of the children who ever filled an antiemetic prescription in the 14 days after the index visit), so did not address children who filled an antiemetic prescription after the index visit.

We chose to limit our investigation of AGE therapy in children to medications that could be fully accounted for and measurably ascribed to AGE treatment. Since antiemetics (as opposed to antimotility agents) require a prescription, we were able to reliably determine usage using a claims-and-encounter database. We excluded antibiotic agents because of the potential that children had a concomitant bacterial process (eg, otitis media) that was not coded on a claims-and-encounter database.

Since it was decided a priori that children younger than 5 years and children younger than 2 years might be clinically important subgroups, separate subgroup analyses were performed. We believed that children younger than 5 years were an important subgroup since the AAP published specific guidelines concerning the treatment of AGE in children of that age. Children younger than 2 years were believed to be an important subgroup because promethazine therapy is not approved for their use. In addition, subgroup analyses were done restricting diagnosis to only those children diagnosed as having viral AGE at the index visit since children who have just vomiting, nonspecific diarrhea, or a bacterial-amebic-parasitic cause for diarrhea might be treated differently.

RESULTS

Overall, parents of 1802 (8.9%) of 20222 children seeking care for AGE had a prescription for an antiemetic filled within 3 days of diagnosis. Few children had more than 1 antiemetic prescription filled within 3 days, resulting in a total of 1813 antiemetic prescriptions filled. Most
Comparison of Children for Whom an Antiemetic Prescription Was or Was Not Filled Within 3 Days of Diagnosis of Acute Gastroenteritis*

<table>
<thead>
<tr>
<th>Variable</th>
<th>Univariate Descriptives of Antiemetic Prescriptions Filled Within 3 Days of Diagnosis</th>
<th>Odds Ratio (95% Confidence Interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Size of subsample</td>
<td>18 420 (91.1)</td>
<td>1802 (8.9)</td>
</tr>
<tr>
<td>Age, mean, y</td>
<td>3.64</td>
<td>5.45</td>
</tr>
<tr>
<td>Male, %</td>
<td>51.7</td>
<td>49.6</td>
</tr>
<tr>
<td>Provider type</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pediatrician</td>
<td>4545 (93.9)</td>
<td>296 (6.1)</td>
</tr>
<tr>
<td>Family physician</td>
<td>3613 (89.6)</td>
<td>418 (10.4)</td>
</tr>
<tr>
<td>General practitioner</td>
<td>1035 (88.9)</td>
<td>129 (11.1)</td>
</tr>
<tr>
<td>Emergency physician</td>
<td>2053 (87.0)</td>
<td>307 (13.0)</td>
</tr>
<tr>
<td>Other</td>
<td>7174 (91.7)</td>
<td>655 (8.3)</td>
</tr>
<tr>
<td>Primary language</td>
<td></td>
<td></td>
</tr>
<tr>
<td>English</td>
<td>13 981 (92.8)</td>
<td>1088 (7.2)</td>
</tr>
<tr>
<td>Spanish</td>
<td>3451 (84.7)</td>
<td>624 (15.3)</td>
</tr>
<tr>
<td>Other</td>
<td>988 (91.7)</td>
<td>90 (8.3)</td>
</tr>
<tr>
<td>Residence</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urban</td>
<td>13 428 (92.9)</td>
<td>1031 (7.1)</td>
</tr>
<tr>
<td>Rural</td>
<td>4992 (86.6)</td>
<td>711 (13.4)</td>
</tr>
</tbody>
</table>

Abbreviation: NA, not applicable.

*Data are given as the number (percentage) of children unless otherwise indicated. Values for statistically significant predictors are given in boldface type.

antiemetic prescriptions filled were for promethazine therapy (92%). Children for whom an antiemetic prescription was filled were older, less likely to be cared for by a pediatrician, spoke Spanish as the primary language, and lived in rural residences (Table).

In the logistic regression model, parents of children with AGE who were treated by emergency physicians (odds ratio [OR], 1.90; 95% confidence interval [CI], 1.60-2.26), general practitioners (OR, 1.53; 95% CI, 1.22-1.92), and family physicians (OR, 1.40; 95% CI, 1.19-1.64) were more likely to fill a prescription for an antiemetic than parents of children who were treated by pediatricians (Table). Parents who had older children were more likely to have an antiemetic prescription filled (OR, 1.09; 95% CI, 1.08-1.10). Speaking Spanish as the primary language (OR, 2.15; 95% CI, 1.92-2.40) was associated with having an antiemetic prescription filled compared with those who spoke English as the primary language. In addition, compared with children living in urban centers, parents of children living in rural areas were more likely to have an antiemetic prescription filled (OR, 1.66; 95% CI, 1.49-1.84).

In the Poisson analysis, controlling for age, provider type, language, and place of residence, no association was seen between antiemetic prescription filling and subsequent visit within 2 weeks (IRR, 1.04; 95% CI, 0.94-1.16). When only subsequent ED visits were assessed, an association between antiemetic prescription filling and subsequent ED visit was seen (IRR, 1.35; 95% CI, 1.07-1.71); those who had an antiemetic prescription filled were more likely to experience a subsequent ED visit. However, no association was seen between antiemetic prescription filling and subsequent hospitalization (IRR, 1.22; 95% CI, 0.79-1.90).

Seven of 1802 children whose parents filled an antiemetic prescription within 3 days of diagnosis of AGE had a subsequent visit for adverse reactions (ICD-9 CM codes for adverse drug effect, extrapyramidal reactions, or allergy). One child had an extrapyramidal reaction, 1 child had an adverse drug effect, and 5 children had an allergic reaction coded. None of the children were subsequently hospitalized. This was not significantly different from children whose parents did not have the prescription filled (97 of 16906 children [OR, 0.68; 95% CI, 0.31-1.46]). No difference in subsequent visits for extrapyramidal reactions was seen between these 2 groups (OR, 0.67; 95% CI, 0.01-5.10).

Subgroup analysis for children younger than 5 years and children younger than 2 years revealed that antiemetic prescription filling for AGE was still common: parents of 964 (6.9%) of 13946 children younger than 5 years who had AGE had an antiemetic prescription filled and parents of 457 (5.1%) of 8446 children younger than 2 years who had AGE had an antiemetic prescription filled. Older age, provider other than a pediatrician, speaking Spanish as the primary language, and rural residency were associated with a higher risk of receiving these medications. No difference in subsequent visits for adverse reactions was seen between children for whom an antiemetic prescription was filled and those who had no prescription filled. No change in our inferences was detected when analysis was limited to only children with viral AGE.

We found that parents of almost 9% of children with AGE had an antiemetic prescription filled within 3 days of the initial diagnosis. Parents of older children, those who are Spanish-speaking, those living in rural locations, and those cared for by emergency physicians, general practitioners, or family practitioners (vs pediatricians) were more...
likely to have prescriptions for antiemetics filled. Children for whom prescriptions for antiemetics were filled had no difference in subsequent visits for adverse reactions potentially related to their use. Overall, there was no association between the number of subsequent visits and the number of antiemetic prescriptions filled, but there was an association between subsequent ED visit and the number of antiemetic prescriptions filled.

Studies in other industrialized countries have shown that while the prevalence of antiemetic prescribing decreased, antiemetics continued to be prescribed for 4.5% to 19% of children admitted to the hospital with AGE.23-28 The only US-based study looking at this issue revealed that a significant proportion of children younger than 6 years were prescribed promethazine therapy (an antiemetic)—14% of hospitalized children and 3.8% of all children with AGE.29 However, that study was conducted in a single staff model health maintenance organization with a history of successfully deploying clinical practice guidelines, so the findings of Christakis et al29 may not be generalizable to children cared for in other settings.

There are several possible explanations for the use of antiemetics despite AAP guidelines. First, practitioners may be unaware of the guidelines, which were published 2 years before data collection on this study began.30,31 In particular, family physicians may be less familiar with the AAP recommendations than pediatricians. Although a synopsis of the AAP guidelines was also published in American Family Physician in 1996, antiemetics are not mentioned in that article.32

A national survey of pediatricians published in 2002 found that 34% were familiar with the AAP guidelines for AGE.31 A national survey of emergency physicians published in 2001 found that 37% were familiar with the AAP practice parameters on AGE in children.33 Since the proportion of pediatricians and emergency physicians familiar with the AAP guidelines are comparable, awareness of the guidelines may not account for the large disparity of prescribing patterns between pediatricians and emergency physicians.

Second, although physicians may be familiar with the AAP guidelines, they may choose not to follow them.30,31 Although 34% of the pediatricians surveyed were familiar with the AGE guidelines, only 9% used them.31 The emergency physician survey found that physicians familiar with the guidelines were more likely to use oral rehydration therapy than their colleagues less familiar with the guidelines, but oral rehydration therapy was still used in only 81% (vs 66%), of children with mild dehydration and 25% (vs 10%) of children with moderate dehydration.33 That study did not ascertain antiemetic use in the treatment of AGE in children.

Third, given the extraordinarily limited studies of antiemetics for children with AGE, physicians may choose to prescribe antiemetics to children based on anecdotal evidence of their efficacy and lack of first-hand knowledge of their potential adverse effect.34-36 Fourth, physicians may respond to perceived patient or parental pressure to prescribe medications.37-41 It is unknown how this would affect antiemetic prescription patterns for AGE.

Emergency physicians who may be more likely to witness adverse reactions to antiemetics are still more likely to prescribe them. Patient characteristics, such as increased symptom severity, may also contribute to a higher proportion of children seen by emergency physicians having an antiemetic prescription filled. Children who are treated in the ED may, as a group, have more severe symptoms than children who are examined in a physician's office.

In addition, subsequent illness course and recovery can only be crudely measured by frequency of return visits to the clinic or ED and subsequent hospitalization. Interpretation of subsequent visits is difficult. In our study, antiemetic prescription filling was associated with increased ED visits, but not with increased hospitalization or increased overall visits. It is likely that children for whom an antiemetic prescription was filled may have more severe symptoms than children who did not. It is also possible that the subsequent ED visits were related to potential adverse effects of the medication that were either unrecognized or not coded for.

There are several limitations to this study. First, the cohort was defined based on the ICD-9 CM code assigned at the time of the initial visit. The accuracy of this diagnosis could not be confirmed. Unfortunately, the clinical severity of AGE, including level of dehydration at presentation, could not be assessed using claims and encounter data.

Second, our study accounts for only prescriptions that are filled, not all prescriptions written. In addition, our study does not capture any medications administered in the office or the ED. We defined our population exposed to antiemetics as those children for whom an antiemetic prescription was filled within 3 days of the index visit for AGE. Parents of some children may have had antiemetic prescriptions filled after this period. Therefore, our study would underestimate the use of antiemetics for AGE in children.

Third, our estimate of adverse effects due to antiemetics may be inaccurate since only those events that warranted a medical visit would be recorded in our database. Children with mild adverse effects could be less likely to present for subsequent care. In addition, since an administrative database does not allow us to interpret adverse events or subsequent health care use until the day after an antiemetic prescription was filled, adverse events that occurred on the day an antiemetic prescription was filled would have been missed.

Fourth, this study was conducted in a single state's Medicaid population. The extent to which prescribing patterns are similar in other states or on other insurance is unknown.
CONCLUSIONS

Antiemetic use in the treatment of AGE is common in children and adverse effects requiring a subsequent visit seem minimal. Further study of the motivation behind antiemetic use for the treatment of AGE in children from both the physician and family viewpoint is warranted. In addition, further study of the safety and efficacy of antiemetics in children may be warranted.

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