Syndromic Surveillance of Gastrointestinal Illness Using Pharmacy Over-the-Counter Sales

A Retrospective Study of Waterborne Outbreaks in Saskatchewan and Ontario

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ABSTRACT

Objective: To ascertain if monitoring over-the-counter (OTC) drug sales could provide a timely syndromic surveillance method of detecting outbreaks of gastrointestinal illness.

Method: This study evaluated the potential of a syndromic surveillance system by comparing retrospective pharmacy OTC sales of anti-nauseants and anti-diarrheals to emergency room visits and case numbers from two Canadian outbreaks related to water contamination by *Cryptosporidium*, and *E.coli* O157:H7 and *Campylobacter*.

Results: Local sales trends of weekly aggregate OTC products were comparable to the outbreak epidemic curves. Statistical control tests on the sales data indicated the start of the outbreak periods.

Conclusions: An automated monitoring tool based on spatial and temporal trend analyses of daily OTC sales would provide supplemental community health information for public health officials that is timelier than currently available laboratory-based surveillance systems.

La traduction du résumé se trouve à la fin de l'article.

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A primary aim of community health surveillance is to provide timely and accurate information on the health status of residents and to prompt public health action. In Canada, most notifiable infectious diseases, including enteric infections, currently are identified through laboratory confirmation. As a result, there is a significant period of time between when patients become ill, seek primary health care and the eventual notification of public health officials. If, for example, an infectious agent is introduced into community water supplies (whether unintentionally or intentionally), this lag time can impede detection of a disease outbreak and implementation of effective interventions to prevent further illnesses or deaths. In addition, several studies discuss the issue of the low proportion of cases that are actually captured throughout reporting chains,¹⁻³ effectively providing health officials with data that underestimate community occurrences. By exploring potential sources of additional information for monitoring community health, syndromic surveillance (surveillance based on an aggregate of signs and symptoms) emerged as a prospective method to identify or verify community-wide increases in different disease syndromes (e.g., diarrheal illness). Several sources of community-level information can be used in this way, such as the monitoring of 911 calls, absenteeism in schools, nurse telehealth calls, emergency room visits and sales of over-the-counter (OTC) drugs.^{4,5}

In this study, we investigated how pharmacy sales trends compared to both the frequency of emergency room visits and identified cases of gastrointestinal illness (GI), by reviewing retrospective data from two Canadian waterborne outbreaks with different disease onset patterns. The primary aim was to explore relationships between pharmacy OTC sales and the epidemic curves; one in the Battlefords area of Saskatchewan (spring of 2001), and the other in Walkerton, Ontario (spring of 2000). Two statistical aberration detection methods were used to assess how early the OTC sales data indicated a potential outbreak was occurring.

METHODS

Data collection – Battlefords, Saskatchewan

An epidemiological investigation of the outbreak of *Cryptosporidium* infections

TABLE I

Data Sources Used for Analyses in This Study

Type of Data	Battlefords, Saskatchewan Waterborne Outbreak: <i>Cryptosporidium</i> Infection	Walkerton, Ontario Waterborne Outbreak: <i>E.coli</i> O157:H7 and <i>Campylobacter</i> Infection
Pharmacy OTC Sales	Anti-diarrheals & Anti-nauseants • Aggregate unit sales* of 4 products, by week (Jan-May 2000 & 2001)	Anti-diarrheals & Anti-nauseants • Aggregate unit sales* of 12 products by week (Jan 1999-Dec 2000) of Walkerton pharmacy
Case-related Data	• Case-series data • Cross-sectional study	• Case-series data • Cross-sectional study
Emergency Room Visit Data	All patients diagnosed with acute GI illness (Feb-May 2001)	All patients diagnosed with acute GI illness/ vomiting/diarrhea (Mar-June 2000)

* Total weekly unit sales of OTC products classified by pharmacist as either anti-diarrheal or anti-nauseant.

that affected individuals from both the City of North Battleford and the Town of Battleford (collectively known as 'the Battlefords') included a descriptive case series study, a randomized cross-sectional study, and an investigation of pharmacy sales of selected OTC products.⁶ The outbreak period lasted from March to May 2001. A subset of information collected for the outbreak investigation, described by Stirling et al.,⁶ is used in this study. Since each of the three pharmacies in the City of North Battleford had different sales inventory periods (either weekly or monthly), data from a pharmacy with weekly summaries of unit sales of four commonly used OTC products related to acute GI were chosen for this study (Table I). A unit sale was described as the sale of one item, regardless of volume (i.e., 100 ml vs. 500 ml) or quantity (i.e., 10 capsule package vs. 100 capsule package). Daily frequencies of Emergency Room (ER) visits of patients diagnosed with acute GI were obtained for February through May 2001.

Data collection – Walkerton, Ontario

Data from a descriptive case series and cross-sectional study,⁷ conducted to investigate a waterborne outbreak that occurred in Walkerton between May and June 2000, were used.

In February 2002, six pharmacies in Walkerton and the surrounding area were asked to provide OTC sales data for the outbreak period. Logistically, only one pharmacy (in Walkerton) was able to supply electronic weekly aggregate unit sales relating to acute GI (anti-nauseants, anti-diarrheals and rehydration products). These were provided for January 1, 1999 to December 31, 2000. In December 2002, the South Bruce Grey Health Centre in Walkerton provided ER visit

Figure 1. A comparison of weekly aggregate unit sales of over-the-counter anti-diarrheals and anti-nauseants with the epidemic curve (a) and emergency room visits (North Battleford Hospital) related to gastrointestinal illness (b) from January to May 2001 in The Battlefords, Saskatchewan.

The epidemic curve indicates the total number of isolate-confirmed cases and epidemiologically-linked cases by reported onset date.

Figure 2. A comparison of weekly aggregate unit sales of over-the-counter anti-diarrheals and anti-nauseants with the epidemic curve (a) and emergency room visits (Walkerton Hospital) related to gastrointestinal illness (b) from March through June 2000 in Walkerton, Ontario.

The epidemic curve indicates the total number of isolate-confirmed cases and epidemiologically-linked cases by reported onset date. Note that the first confirmed isolate of *E.coli* O157:H7 was reported to the local Health Unit on May 20, 2000.

information as daily aggregate counts of patients diagnosed with diarrhea, vomiting or acute gastrointestinal illness for the period of March through June 2000. A summary of data used in this study is given in Table I.

Comparing the epidemic curve, unit sales of OTC products and emergency room visits

Epidemic curves for both the Battlefords and the Walkerton outbreak were based on case numbers by onset date derived from the case series investigations. Weekly

aggregate unit sales of OTC anti-diarrheals and anti-nauseants, plotted by the end of the sales week date, were produced for each pharmacy. The daily frequency of ER visits (by visit date) related to acute GI was also plotted for the two outbreaks.

CUSUM and moving average in detecting aberrations

Two statistical control methods were applied to 2 years of aggregate weekly sales data (January 1999 through December 2000) from the Walkerton pharmacy, in order to detect aberrations in sales events over time.

The Cumulative Sum (CUSUM), which requires historical information, and simple Moving Average (MA) analyses were run using the SAS[®] statistical package.⁸ The threshold for the CUSUM was set at $h=2$; for the Moving Average (span of 2), three standard deviations from the mean defined the limits. Details on these algorithms may be obtained elsewhere.⁹⁻¹¹

RESULTS

The Battlefords

Figure 1a shows the epidemic curve (number of cases plotted by onset date) and combined weekly aggregate unit sales of OTC anti-diarrheals and anti-nauseants in the weeks up to and including the outbreak period. The plot includes cases that occurred prior to ($n=119$), and during the outbreak period ($n=1039$). In total, 10.6% of outbreak-related cases were reported (laboratory-confirmed) to the Public Health Unit; the remaining epidemiologically linked cases (not laboratory-confirmed) were identified retrospectively through investigative surveys.

A dramatic increase in OTC sales is shown during the outbreak period. OTC sales data were also plotted against the frequency of ER visits of patients diagnosed with acute GI (Figure 1b). The increasing trend evidenced at the start of the outbreak period in both the OTC sales and epidemic curve is not obvious in the more variable ER visits trend line.

Walkerton

Figure 2a compares weekly aggregate OTC unit sales of anti-diarrheals and anti-nauseants with the epidemic curve, which included all cases that were epidemiologically linked to the outbreak.

The sharp drop in unit sales after the week ending the 26th of May was a result of pharmacists halting purchases of products related to GI on the 20th of May, except upon consultation with a pharmacist. A comparison of OTC sales with the frequency of patients visiting the Walkerton hospital ER, and diagnosed with GI, is found in Figure 2b. Sales were seen to rise sharply at the same time as the epidemic curve, but ER visits did not show an obvious increase until well after the large spikes in both the OTC sales trend and the epidemic curve.

Statistical algorithms applied to OTC sales data for aberration detection

Moving Average (MA) and CUSUM plots using the weekly aggregate sales data of GI-related products from the Walkerton pharmacy are shown in Figures 3 and 4 respectively. Points are plotted by the end of the weekly sales period (Saturday through Friday) dates. Both statistical control methods detected significantly high sales for the same two periods over these 24 months. In December of 1999, the CUSUM trend line crossed the threshold for two consecutive weeks (ending the 24th and the 31st). The MA also showed high sales for these two periods, with the trend line approaching the upper limit the week ending the 24th, and surpassing it the week ending the 31st. Total unit sales for these two weeks were 53 and 37 respectively.

The next period of significantly increased sales was during the May 2000 outbreak. Symptom onset dates were reported as starting around the 13th of May; numbers of cases quickly escalated in the days following. Trend lines from both the MA and the CUSUM climbed for the sales week ending the 19th, and then spiked sharply, greatly exceeding the upper boundary lines for the sales week ending the 26th. Of note is that since GI-related product sales were halted by the afternoon of the 20th and the store was closed on the 21st and 22nd, the major spike reflected predominantly sales from the morning of the 20th. Total sales for the weeks ending the 19th and the 26th were 49 and 74 units, respectively. In comparison, average weekly sales in the four weeks prior to the outbreak were 23 units. Excluding the four periods of high sales, weekly aggregate sales over the two years of data ranged from 11 to 45 units.

DISCUSSION

In Canada, there is currently no organized system that uses syndromic data, such as pharmacy OTC sales, for community health surveillance. Our study supports the hypothesis that monitoring OTC sales activities of certain drugs gives an indication of GI-related events in the community, and thus can provide vital information for public health, in the form of systematic observation of trends. This is particularly important in situations where infected

Figure 3. Moving Average (MA) chart (span of 2), using two years of weekly aggregate sales (1999-2000) of OTC anti-nauseant and anti-diarrheal products from a Walkerton pharmacy. Aberrant sales are indicated when the MA exceeds 3 standard deviations.

Figure 4. Cumulative Sum (CUSUM) technique using a Walkerton pharmacy's sales of OTC products relating to gastrointestinal illness (weekly aggregate counts for 1999-2000). The system is seen to be 'out of control' when the curve crosses the dashed line (CUSUM threshold).

individuals have symptoms prompting self-medication, rather than going to a private practice or emergency room physician, as was evidenced in the Battlefords outbreak trends. Under these circumstances, OTC sales trends would provide a more sensitive, timely and geographically specific detection tool than is available through monitoring ER visits or the slower laboratory-based surveillance. It is important to remember that though cases are plotted by onset date, public health officials would not receive notification of these reportable

isolate occurrences until at least several days later. Though sales patterns of OTC products showed a definitive increase at the same time as onset dates of outbreak-related cases in both outbreaks discussed here, there is a key difference between the two. The speed and magnitude of the waterborne outbreak related to contamination by *E.coli* O157:H7 and *Campylobacter* in Walkerton was reflected in the correspondingly large and rapid increase in sales of related OTC products in the same week. In the Battlefords, the more pro-

longed period of elevated OTC drug sales reflected the almost 90% of unreported cases during the outbreak, many of whom were self-medicating in response to the less severe symptoms of *Cryptosporidium* infection.

A relationship between pharmacy OTC sales data and epidemic curves (related to GI) has been documented for several waterborne outbreaks.¹²⁻¹⁶ The statistical control tests used in this study simply demonstrated the utility of aberration detection methodology. However, adaptations to these and more sophisticated algorithms, such as the Early Aberration Reporting System (EARS),^{17,18} time series methods, neural networks and spatial modelling, will have to be developed to adjust for a number of factors contributing to the general noisiness of these data, such as seasonal effects, promotional sales, pharmacy attributes, and type of population served. A limitation of this study was sales data availability, emphasizing the need to determine the required number of representative sites for an area necessary for describing different sales patterns aberrations (i.e., increased sales in three area pharmacies versus one pharmacy with increased sales for three days). Geo-referencing these data will allow for patterns of disease occurrence to be described through a number of spatio-temporal analytical techniques, which would be useful for public health prevention and intervention planning.

This study utilized retrospectively collected sales information to illustrate the usefulness of these data for real-time syndromic surveillance. To implement such a system at the community, provincial or national level will necessarily require a timely and consistent transfer and analysis of information to adequately monitor the target populations. Past attempts at using sales data supplied by phone or fax failed mainly due to limitations of time and personnel,¹⁹ so the success of such a system will rely on automating collection, analysis and dissemination of results to the appropriate health officials in a way which is useful to them. Major Canadian retailers have sophisticated, centralized database reg-

istries for electronic daily and historical stock keeping, so the feasibility of an automated surveillance system should be explored at this time.

In conclusion, syndrome-based monitoring of OTC sales offers a simple and effective tool to enhance the ability of public health officials to detect trends and aberrations in community health, give a sense of the geographical area affected in outbreak situations, and provide historical patterns that would aid in planning preparedness and targeted interventions.

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RÉSUMÉ

Objectif : Vérifier si la surveillance des ventes de médicaments en vente libre pourrait être une méthode de surveillance syndromique opportune en vue de détecter les éclosions de maladies gastro-intestinales.

Méthode : Nous avons évalué les possibilités d'un système de surveillance syndromique en comparant les ventes rétrospectives d'antinauséux et d'anti diarrhéiques vendus librement en pharmacie aux visites en salles d'urgence et au nombre de cas associés à deux éclosions au Canada liées à la contamination de l'eau par *Cryptosporidium*, et par *E.coli* O157:H7 et *Campylobacter*.

Résultats : Les tendances des ventes locales hebdomadaires de produits en vente libre suivaient les courbes des flambées épidémiques. Des contrôles statistiques des chiffres de vente ont indiqué le début des périodes d'éclosion.

Conclusion : Un outil de surveillance automatique basé sur l'analyse des tendances spatiales et temporelles des ventes quotidiennes de médicaments en vente libre fournirait aux agents de santé publique des renseignements supplémentaires sur la santé communautaire plus à jour que les systèmes de surveillance actuellement utilisés par les laboratoires.