Availability of antidotes at acute care hospitals in Ontario

Research

Recherche

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Abstract

Background: Acutely poisoned patients sometimes require immediate treatment with an antidote, and delays in treatment can be fatal. We sought to determine the availability of 10 antidotes at acute care hospitals in Ontario.

Methods: Mailed questionnaire with repeated reminders to pharmacy directors at all acute care hospitals in Ontario.

Results: Responses were obtained from 179 (97%) of 184 hospitals. Only 9% of the hospitals stocked an adequate supply of digoxin immune Fab antibody fragments, a life-saving antidote for patients with severe digoxin toxicity, whereas most of the hospitals stocked sufficient supplies of ipecac syrup (88%) and flumazenil (92%), arguably the least crucial antidotes in the survey. Only 1 hospital stocked adequate amounts of all 10 antidotes. Certain hospital characteristics were associated with adequate antidote stocking (increased annual emergency department volume, teaching hospital status and designation as a trauma centre). Conversely, antidote supplies were particularly deficient at small hospitals and, paradoxically, geographically isolated facilities (those most reliant on their own inventory). The cost of antidotes correlated only weakly with stocking rates, and many examples of excessive antidote stocking were identified.

Interpretation: Most acute care hospitals in Ontario do not stock even minimally adequate amounts of several emergency antidotes, possibly jeopardizing the survival of an acutely poisoned patient. Much of this problem could be rectified at no additional cost by reducing excessive stock of expensive antidotes and redistributing the resources to acquire deficient antidotes.

Drugs and poisons are responsible for about 1 death each day in Ontario.[1] Acutely poisoned patients usually require emergency care, and some require swift administration of an antidote. The treatment of digoxin-induced arrhythmias with digoxin immune Fab antibody fragments is a specific example in which a delay in antidote administration may prove fatal.[2]

Despite the effectiveness of digoxin immune Fab, a recent survey of 108 hospitals in the Unites States found that only 2% stocked enough of the antidote to treat a single severe adult poisoning.[3] Many other effective antidotes were also inadequately stocked, a finding confirmed by investigators elsewhere.[4,5]

We sought to determine whether the problem of inadequate antidote supplies prevails within our hospital system despite differences in hospital administration and funding between the United States and Canada.

Methods

We mailed a 1-page questionnaire to the pharmacy directors of all acute care hospitals in Ontario in September 1999. A second mailing was sent to nonrespondents in November 1999, followed by faxed reminders in January 2000. Eligible hospitals (those with active emergency departments) were identified from the Ontario Hospital Association (OHA)[6] and cross-referenced with records at the Institute for Clinical Evaluative Sciences (ICES). For facilities with multiple sites and emergency departments, each site was treated as a separate hospital. Eligible hospitals were categorized as teaching, small or community hospitals ac-

cording to the classifications of the Joint Policy and Planning Committee (JPPC).[7] The JPPC defined teaching hospitals as those on the member list of the Ontario Council of Teaching Hospitals, small hospitals as those with a referral population of less than 20 000 and fewer than 50 inpatient beds, and community hospitals as those not classed as small or teaching hospitals. In addition, 13 of the hospitals were designated as regional trauma centres, according to the Ontario Trauma Registry.[8]

We estimated each hospital's annual emergency department volume using OHIP billing records. To determine whether proximity to another institution influenced antidote supply, each hospital's latitude and longitude were obtained from its postal code and used to calculate the distance to the nearest facility.[9]

Pharmacy directors were asked to report the amount of each of 10 antidotes (Table 1) currently in stock anywhere in their hospital. We chose 8 of these antidotes because their immediate use can reduce poisoning-related morbidity and mortality.[10–17] Two other antidotes (syrup of ipecac and flumazenil) were included for comparison because, although they have a role in the management of some poisonings, alternatives are available and often preferable.[18,19]

Despite their importance, we chose not to include atropine and naloxone because they are often distributed widely throughout hospitals and are therefore difficult to enumerate, which might have led to invalid estimates and reduced response rates. Also, we did not include *N*-acetylcysteine (for acetaminophen overdose) because a treatment delay of 1–2 hours is unlikely to influence patient outcome adversely.[20,21]

For each hospital, we categorized the supply of each antidote as either adequate or inadequate. Because no universally accepted guidelines exist to define adequacy, we obtained suggested amounts from a standard toxicology text and previous surveys.[4,5,10–19] These amounts represent the approximate quantity of antidote needed to initiate treatment of 1 case of severe poisoning in an adult and are generally more conservative than amounts in recently published guidelines intended to ensure adequate supplies for 4 hours of treatment for 1 or 2 patients.[22] For many poisonings, the amount of antidote needed to complete therapy is often considerably greater.

Estimating a 75% response rate, our sample size was designed to have an 80% power of obtaining a 95% confidence interval with a width of less than 10% for the point estimate of the proportion of hospitals adequately stocked with all 10 antidotes. We performed a univariate analysis to test for an association between hospital characteristics and the adequacy of antidote stocking. The dependent variable was the number of adequately stocked antidotes (0–10) at each site. Characteristics found to be associated with antidote stocking were incorporated into a linear regression model to identify independent predictors of antidote supply. All analyses used a 2-tailed p value of 0.05 to define statistical significance.

Table 1: Antidotes included in the survey of antidote supplies in Ontario's acute care hospitals

Antidote	Poisoning indication	Minimum stocking amount*
Deferoximine	Iron	1 g
Digoxin immune Fab	Cardiac glycosides	20 vials
Ethanol (parenteral)	Methanol, ethylene glycol	70 g
Flumazenil	Benzodiazepines	1.5 mg
Glucagon	β-Blockers	20 mg
Methylene blue	Methemoglobinemia	150 mg
Pralidoxime	Organophosphates	2 g
Pyridoxine (injection)	Isoniazid	5 g
Sodium thiosulfate†	Cyanide	25 g
Syrup of ipecac	Various	60 mL

*Amount needed for initial treatment of 1 case of severe poisoning in an adult.
†Component of cyanide antidote kit.

Results

We received responses from 179 (97%) of the 184 hospitals sent the questionnaire. The typical hospital was small, located about 18 km from the nearest facility and treated over 17 000 patients in the emergency department annually. The characteristics of respondents and nonrespondents were similar (Table 2).

Only 1 hospital (0.6%) was adequately stocked with all 10 antidotes. Most of the hospitals had adequate supplies of flumazenil (92%) and syrup of ipecac (88%), arguably the least essential antidotes in the survey (Table 3). By comparison, few hospitals (9%) had a sufficient amount of digoxin immune Fab to treat 1 case of severe poisoning. Indeed, the majority (59%) reported having none of the antidote in stock, including 6 teaching hospitals and 25 hospitals with 20 000 or more emergency visits each year.

Characteristics associated with adequate antidote stocking were increased annual emergency department volume (about 1 more antidote per 10 000 patient visits), teaching hospital status (about 2 more antidotes than nonteaching sites) and designation as a trauma centre (about 3 more antidotes than nontrauma centres) (Table 4). Small hospitals stocked about half as many antidotes as the larger centres stocked. Paradoxically, increased distance from the nearest facility was associated with deficient antidote stocking (about 1 less antidote per 40 km to the nearest facility).

Table 2: Characteristics of acute care hospitals in Ontario

Characteristic	Respondents *n = 179*	Nonrespondents *n = 5*
Hospital type*		
Teaching	23	1
Community	65	2
Small	91	2
Regional trauma centre	13	0
Annual ED volume		
Median	17 784	32 057
Minimum	352	400
Maximum	70 000	50 605
Distance to nearest facility, km		
Median	17.9	5.6
Minimum	0.1	0.6
Maximum	132.3	39.8

Note: ED = emergency department.
*The number of respondents totals more than 179 because of the overlap with the category "regional trauma centre."

In the multivariate analysis, increased annual emergency department volume and designation as a trauma centre were independent predictors of adequate antidote stocking, and small hospital status was an independent predictor of poorer antidote supply. The regression model explained 49% of the variance in stocking adequacy. We found only a weak correlation between acquisition cost and the adequacy of antidote supply ($r_s = -0.50$, $p = 0.14$).

Many of the hospitals had an abundance of certain antidotes, particularly flumazenil, despite a complete lack of others, including the relatively inexpensive antidotes deferoximine, pralidoxime and sodium thiosulfate. Although most of the hospitals were poorly stocked with antidotes, some examples of gross overstocking were also apparent. One small hospital reported having 50 vials of digoxin immune Fab on hand, worth more than $20 000. Fifty-five hospitals had at least 1000 mg of methylene blue on hand, with one facility prepared for the simultaneous presentation of 37 adults with methemoglobinemia. Twenty-six hospitals each stocked between 200 and 710 mL of flumazenil, the aggregate cost of which approached $50 000.

Interpretation

Our survey of acute care hospitals in Ontario revealed that many poisoning antidotes are not stocked in adequate quantities for the initial treatment of even 1 case of severe poisoning. Of the 10 antidotes we evaluated, the 2 most often stocked adequately were flumazenil and syrup of ipecac, the antidotes least likely to be lifesaving in an emergency. In contrast, digoxin immune Fab is unquestionably effective in cases of severe digoxin poisoning,[2,23] and yet over half of the hospitals did not stock it and one-third had insufficient supplies.

The definition of how much antidote is adequate is debatable. We purposely selected amounts that might be needed during the first hour. Early treatment is crucial for most of the antidotes in our survey. Had we instead asked about larger amounts recommended for use in the first 24 hours,[24] the rates of insufficiency would have been much more striking.

Several respondents indicated that a borrowing agreement existed with nearby hospitals, usually for digoxin immune Fab. Although this may be a financially attractive option, the wisdom of such a practice is questionable because of the time required to obtain the drug. For a patient with serious digoxin-induced arrhythmias, even 30 minutes spent procuring the antidote could prove fatal. Furthermore, we found that geographically isolated facilities (those most reliant on their own inventory) were the least likely to be adequately stocked.

The acquisition cost may influence the stocking of some antidotes, yet we found only a weak correlation between cost and the adequacy of antidote supply. Concern about expiration of infrequently used antidotes is irrelevant because most are stable for several years. Furthermore, suppliers will usually issue credit for outdated product.

The extent of overstocking in some cases was surprising. For perspective, imposing a theoretical target of antidote supply equal to 3 times the minimum amount we established for the study, with each site redistributing the excess expenditures to its own deficient antidotes, would allow 46 hospitals to stock 2 more of the 8 essential antidotes (excluding ipecac and flumazenil) adequately. Another 21 hospitals could stock 4 more antidotes adequately. In all, 150 of the 179 hospitals could improve their stocking adequacy by 2.6 antidotes on average (range 1–7), almost doubling the overall adequacy rate for these 8 antidotes, from 34% (493/1432) to 64% (914/1432).

Our study had several limitations. First, we relied on self-reported data. There is no apparent reason why intentional underestimation of antidote stocks should occur, however, and social desirability bias may have led some of

Table 3: Antidote-specific stocking rates and acquisition costs

Antidote	Stocking rate, %*	Acquisition cost, $†
Deferoximine	55	26
Digoxin immune Fab	9	8241
Ethanol (parenteral)	62	53
Flumazenil	92	84
Glucagon	32	657
Methylene blue	74	11
Pralidoxime	27	50
Pyridoxine (injection)	23	89
Sodium thiosulfate	18	50
Syrup of ipecac	88	6

*The proportion of hospitals with at least the minimum stocking amount (Table 1) on hand.
†Approximate cost for enough antidote to treat 1 case of severe poisoning in an adult (initial treatment only; about 1 hour), expressed in 1999 Canadian dollars. The manufacturer's list price is used for antidotes with a single manufacturer; the cost to Sunnybrook & Women's College Health Sciences Centre is used for antidotes with multiple manufacturers.

Table 4: Hospital characteristics associated with antidote supply*

Hospital characteristic	Regression coefficient (and 95% CI)
Univariate analysis	
Annual ED volume (per 10 000 visits)	0.94 (0.79 to 1.10)
Teaching facility	1.93 (1.02 to 2.85)
Small hospital	–2.62 (–3.13 to –2.11)
Regional trauma centre	2.96 (1.81 to 4.12)
Distance to nearest facility (per 100 km)	–2.56 (–3.74 to –1.37)
Multivariate analysis	
Annual ED volume (per 10 000 visits)	0.63 (0.40 to 0.86)
Regional trauma centre	1.14 (0.04 to 2.23)
Small hospital	–0.99 (–1.73 to –0.26)

Note: CI = confidence interval.
*Dependent variable is the number of adequately stocked antidotes (0–10) at each site.

the respondents to overstate their supplies. Second, some hospitals did not respond to our survey. However, even if all of the nonrespondents were fully stocked, the overall adequacy rate would still be only 3%. Finally, it was not possible to examine antidote usage patterns; however, most of the antidotes surveyed are needed infrequently.[25] Nevertheless, reliance on probabilities to guide emergency preparedness is a dangerous practice for obvious reasons.

To summarize, many acute care hospitals in Ontario do not maintain minimally adequate supplies of several essential antidotes and are therefore ill-prepared to manage specific toxicologic emergencies. Redistribution of resources at some hospitals could improve these deficiencies at no additional cost.

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