Antidote stocking in British Columbia hospitals

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ABSTRACT

Introduction: Previous studies have demonstrated that antidotes are insufficiently stocked in Canadian and US health care facilities. The purpose of this study was to determine the adequacy of antidote stocking in British Columbia hospitals based on the current guidelines.

Methods: A written survey was mailed to hospital pharmacy directors at all 93 acute care facilities in BC. Availability of 14 essential antidotes was classified as sufficient or insufficient based on the current guidelines. Facilities were stratified into small (<50 beds), medium (50–250 beds) or large (>250 beds); teaching or non-teaching; trauma or non-trauma, urban or rural, and isolated or non-isolated.

Results: Complete responses were received from 75 (81%) of 93 hospitals. No hospital had adequate stock of all 14 antidotes. Overall, the average number (± standard deviation) of antidotes adequately stocked was 4.2 ± 2.9 per hospital. Urban hospitals had adequate stocks of 6.5 ± 2.6 antidotes while rural centres had adequate stocks of 2.6 ± 1.8 ($p < 0.001$). Corresponding figures were 9.0 ± 1.8 for teaching hospitals vs. 3.7 ± 2.4 for non-teaching hospitals ($p < 0.001$), 8.9 ± 2.0 for trauma centres vs. 3.8 ± 2.5 non-trauma centres ($p < 0.001$), and 2.5 ± 2.1 for isolated hospitals vs. 4.6 ± 2.9 for non-isolated hospitals ($p = 0.018$). Small, medium, and large hospitals adequately stocked 2.3 ± 1.7, 5.7 ± 2.2, and 7.7 ± 3.0 antidotes, respectively ($p < 0.001$). The 4 antidotes most adequately stocked were sodium bicarbonate (77%), *N*-acetylcysteine (64%), ethanol (49%) and naloxone (47%). Digoxin immune F_{ab} fragments, glucagon, pyridoxine and rattlesnake antivenin were poorly stocked with sufficient supplies of 5%, 7%, 7% and 13%, respectively.

Conclusion: BC hospitals do not have adequate antidote stocks. Provincial stocking guidelines and coordination of antidote purchasing and stocking are necessary to correct these deficiencies.

Key words: antidote, overdose, toxicology, poisoning

RÉSUMÉ

Introduction : Des études antérieures ont démontré une réserve insuffisante d'antidotes dans les services de santé canadiens et américains. La présente étude avait comme objectif de déterminer si, en se basant sur les directives existantes, les réserves d'antidotes dans les hôpitaux de la Colombie-Britannique sont suffisantes.

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Méthodes : Un sondage par écrit fut posté aux directeurs de pharmacie des 93 établissements de soins aigus de la C.-B. La disponibilité de 14 antidotes essentiels fut classifiée comme suffisante ou insuffisante à partir des directives existantes. Les établissements furent stratifiés de la façon suivante : petite taille (< 50 lits), taille moyenne (50–250 lits) ou grande taille (> 250 lits); centre de trauma ou non, urbain ou rural; isolé ou non.

Résultats : Soixante-quinze des 93 hôpitaux (81 %) répondirent au sondage au complet. Aucun hôpital n'avait une réserve adéquate des 14 antidotes. En général, le nombre moyen d'antidotes (± déviation standard) dont les réserves étaient suffisantes était de 4,2 ± 2,9 par hôpital. Les hôpitaux urbains avaient des réserves adéquates pour 6,5 ± 2,6 antidotes, tandis que les centres ruraux avaient des réserves adéquates pour 2,6 ± 1,8 antidotes ($p < 0,001$). Les chiffres correspondants étaient 9,0 ± 1,8 pour les hôpitaux universitaires vs 3,7 ± 2,4 pour les hôpitaux non universitaires ($p < 0,001$), de 8,9 ± 2,0 pour les centres de trauma vs 3,8 ± 2,5 pour les autres centres ($p < 0,001$), de 2,5 ± 2,1 pour les hôpitaux isolés vs 4,6 ± 2,9 pour les hôpitaux non isolés ($p = 0,018$). Les hôpitaux de petite, moyenne et grande taille avaient des réserves suffisantes pour 2,3 ± 1,7, 5,7± 2,2 et 7,7 ± 3,0 antidotes respectivement ($p < 0,001$). Les quatre antidotes dont les réserves étaient les plus adéquates étaient le bicarbonate de sodium (77 %), le *N*-acétylcystéine (64 %), l'éthanol (49 %) et le naloxone (47 %). Les réserves des antidotes suivants étaient insuffisantes : anticorps spécifique de la digoxine (5 %), glucagon (7 %), pyridoxine (7 %) et antivenin pour crotalidae (13 %).

Conclusion : Les hôpitaux de la Colombie-Britannique n'ont pas de réserves d'antidotes en quantités suffisantes. Des directives provinciales d'approvisionnement et la coordination de l'achat et de la réserve des antidotes sont nécessaires pour corriger ces lacunes.

Introduction

In 2000, there were 303 deaths in British Columbia attributed to drugs or toxins.[1] Most poisoned patients can be managed successfully with gastric decontamination and supportive care; however, for some patients, timely administration of the correct antidote is essential to minimize morbidity or prevent deaths. Thus, hospitals that treat poisoned patients must maintain adequate antidote stocks to ensure timely administration.[2] British Columbia encompasses a vast geographical area with rugged mountainous terrain and harsh climate. These geographic factors add to the difficulty of moving patients or antidotes from one hospital to another. This means that even a small centre may be required to treat an acutely ill, poisoned patient for several hours, using only in-hospital supplies.

Over the past 15 years, many studies have demonstrated that antidotes are insufficiently stocked in health care facilities.[3–9] In 2000, Dart and colleagues published the first evidence-based consensus guidelines for stocking antidotes in the United States. These guidelines recommend that 16 essential antidotes should be stocked in all health care facilities that treat acutely poisoned patients.[2] Antidotes were considered essential if they are both effective and necessary within 1 hour of patient presentation. The quantity of antidote recommended was based on the dose necessary to treat 1 or 2 70-kg patients for the first 4 hours (after which a hospital could transfer the patient to another centre or replenish its antidote supply). The purpose of the present study was to determine the proportion of BC hospitals that meet current US antidote stocking guidelines.

Methods

A listing of all BC hospitals was obtained from the BC Ministry of Health (MOH). A 4-part written survey was mailed to hospital pharmacy directors of all 93 acute care facilities in BC in September 1998. Survey data were collated and, in November 2000, telephone follow-up was performed to collect missing data. Multiple attempts were made to contact non-responders and partial responders.

Hospitals surveyed

The hospitals surveyed ranged from small community health care centres to large tertiary care institutions. Health care facilities consisting of multiple sites were treated as separate hospitals. The study excluded cancer agencies, military hospitals, Red Cross outpost hospitals and diagnostic or treatments centres that lack in-patient beds. Facilities were divided into teaching versus non-teaching, trauma versus non-trauma centres, urban versus rural, and isolated versus non-isolated. Urban hospitals were defined as having a referral population of greater than 20 000. Hospitals were considered isolated if they were located more than 100 km by road from another health care centre. Distances were obtained from a driving distance calculator and a Canadian road atlas (www.mapquest.com; click on "driving directions"). The institutions included in this study were strati-

fied into small (<50 beds), medium (50–250 beds) and large (>250 beds) hospitals. Hospital referral areas and bed numbers were obtained from the BC MOH. Hospital categorization was defined explicitly a priori.

Data

Survey data included hospital demographics, laboratory capabilities (particularly those relevant to the management of poisoned patients), antidote quantities stocked, and special antidote requirements related to local industry or venomous animals. The survey was developed prior to US antidote stocking guidelines and captured data on 24 antidotes and gastrointestinal decontamination products, including activated charcoal, atropine, calcium edetic acid (EDTA), calcium gluconate, cyanide antidote kit (amyl nitrite/sodium thiosulfate), deferoxamine, digoxin immune F_{ab} fragments, dimercaprol, ethanol, folic acid, flumazenil, glucagon, calcium gluconate gel (for hydrofluoric acid exposures), syrup of ipecac, leucovorin, methylene blue, *N*-acetylcysteine, naloxone, penicillamine, polyethylene glycol electrolyte solution, pyridoxine, polyvalent rattlesnake antivenin, sodium bicarbonate and thiamine.

For study purposes, we limited our attention to 14 of the 16 antidotes deemed essential in the recently published consensus guidelines (Table 1).[2] Pralidoxime and fomepizole are not discussed here because pralidoxime was not included on the 1998 hospital survey and fomepizole was not available in Canada at the time of the survey. Instead, we looked at the availability of ethanol, an acceptable alternative to fomepizole for toxic alcohol ingestions. Antidote supply for each hospital was classified as sufficient or insufficient based on the consensus guidelines.[2]

Statistical analysis

All data were entered into an Excel 2000 database (Microsoft,® Redmond, Wash.). Two-group comparisons of proportion of antidotes available between various hospital categories were made using the Student's *t*-test. All tests were two-tailed, and Bonferroni's correction was used to adjust for multiple comparisons, resulting in a p value for statistical significance of 0.0125. Comparison of antidote availability between small, medium and large hospitals was done using a one-way analysis of variance (ANOVA) with a p value for statistical significance of 0.05.

Results

Overall, 86 (92%) of 93 health care facilities responded to the survey. Of these, 75 (87%) returned complete information on antidotes stocked; therefore, 75 (81%) of 93 surveyed facilities were included in the final analysis. All 7 of the non-responding hospitals were non-teaching, non-trauma centres. Five were small, 1 was medium-sized and 1 large. Two of the non-responders were urban. All 11 partial responders were small, non-teaching, non-trauma centres, and only 1 partial responder was urban. Table 2 summarizes hospital characteristics.

Figure 1 shows that no hospital had adequate stocks of

Table 1. Individual antidotes, quantities and cost for agents included in the study[2]

Antidote	Indication	Dose required to treat one 70-kg adult	Supply required, no. of patients	Acquisition cost, $Cdn*
N-acetylcysteine	Acetaminophen	21 g	2	89.25
Atropine sulfate	Organophosphates	75 mg	2	35.00
Calcium gluconate	Hydrogen fluoride / CCB	100 mEq	2	17.60
Cyanide kit	Cyanide	1 kit	2	457.60
Deferoxamine	Iron	8.4 g	1	120.70
Digoxin immune F_{ab}	Digoxin	15 vials	1	6 181.20
Dimercaprol	Arsenic / Mercury / Lead	280 mg	1	260.00
Ethanol (100%)	Methanol / EG	90.7 mL	2	170.81
Glucagon	Beta-antagonist / CCB	50 mg	1	1 163.50
Methylene blue	Methemoglobinemia	140 mg	2	60.48
Naloxone	Opioids	15 mg	2	116.10
Pyridoxine	Isoniazid	10 g	1	190.00
Rattlesnake antivenin	Crotalid snakes	10 vials	1	2 469.00
Sodium bicarbonate	TCA / Cocaine / Salicylates	500 mEq	1	59.50
Total expenditure				**11 390.74**

CCB = calcium channel blocker, EG = ethylene glycol, TCA = tricyclic antidepressant
*Acquisition cost obtained from Vancouver General Hospital (2002 Canadian dollars)

all 14 antidotes, although 1 adequately stocked 13. The remaining centres adequately stocked fewer than 10 antidotes, and most (59%) adequately stocked fewer than 5 antidotes. Seven percent (all isolated rural hospitals) had an inadequate supply of all essential antidotes. Table 3 shows that the average number (± standard deviation) of antidotes adequately stocked was 4.2 ± 2.9 per hospital. Urban hospitals had adequate stocks of 6.5 ± 2.6 antidotes while rural centres had adequate stocks of 2.6 ± 1.8 ($p < 0.001$). Corresponding figures were 9.0 ± 1.8 for teaching hospitals vs. 3.7 ± 2.4 for non-teaching hospitals ($p < 0.001$), 8.9 ± 2.0 for trauma centres vs. 3.8 ± 2.5 non-trauma centres ($p < 0.001$), and 2.5 ± 2.1 for isolated hospitals vs. 4.6 ± 2.9 for non-isolated hospitals ($p = 0.018$). Small, medium, and large hospitals adequately stocked 2.3 ± 1.7, 5.7 ± 2.2, and 7.7 ± 3.0 antidotes, respectively ($p < 0.001$). Table 4 shows that the antidotes most often adequately stocked were sodium bicarbonate (77%), *N*-acetylcysteine (64%), ethanol (49%) and naloxone (47%). Conversely, digoxin immune F_{ab} fragments, glucagon, pyridoxine, and rattlesnake antivenin were adequately stocked in only 5%, 7%, 7% and 13% of facilities respectively.

Discussion

No BC hospital met the current consensus recommendations for antidote stocking and most centres had inadequate stocks of 10 or more essential antidotes. Antidote supplies were more likely to be insufficient in smaller, rural, non-teaching and non-trauma hospitals; however, larger urban teaching hospitals were also associated with significant understocking. This situation may place poisoned patients at risk of suffering avoidable morbidity or mortality.

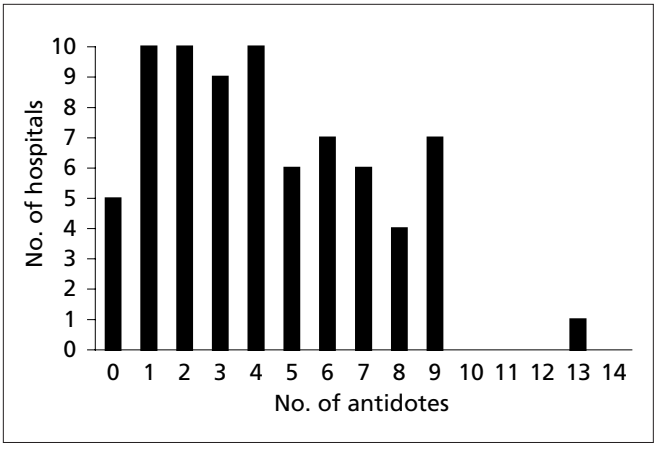

Fig. 1. The x-axis represents the amount of antidotes stocked ranging from 0 to 14 and the y-axis represents the number of hospitals stocking sufficient quantities of antidotes.

Essential antidotes?

Our study is the first to compare provincial antidote stocking to an established consensus guideline, but its results are similar to those of other US studies, which suggest antidote stocking is often inadequate.[3,4,6,7] In a recent Canadian study from Ontario, only 1 of 179 surveyed hospitals stocked adequate amounts of all 10 antidotes evaluated,[8] while in a similar study from Quebec,[9] the median number of adequately stocked antidotes was 3. But what is considered essential — and how much of it — may vary among settings. Regional factors are important when applying guidelines and determining antidote needs; therefore, the antidotes and quantities recommended in the consensus guideline may not be appropriate for all BC hospitals (e.g., rattlesnake antivenin, dimercaprol).

Table 2. Characteristics of hospitals that provided a complete response (*N* = 75)

Characteristic	No. of hospitals (%)
Size (no. of beds)*	
Small (<50)	38 (51)
Medium (50–250)	27 (36)
Large (>250)	10 (13)
Trauma centre	7 (9)
Non-trauma centre	68 (91)
Teaching	8 (11)
Non-teaching	67 (89)
Urban	32 (43)
Rural	43 (57)
Isolated	13 (17)
Non-isolated	62 (83)

* The mean no. of inpatient beds was 123.

Table 3. Mean (± SD) number of antidotes stocked stratified by hospital characteristics (*N* = 75)

Hospital characteristic	Antidotes stocked	*p* value
Overall	4.2 ± 2.9	–
Teaching	9.0 ± 1.8	<0.001
Non-teaching	3.7 ± 2.4	
Urban	6.5 ± 2.6	<0.001
Rural	2.6 ± 1.8	
Trauma	8.9 ± 2.0	<0.001
Non-trauma	3.8 ± 2.5	
Non-isolated	4.6 ± 2.9	<0.018
Isolated	2.5 ± 2.1	
Small	2.3 ± 1.7	
Medium	5.7 ± 2.2	<0.001
Large	7.7 ± 3.0	

If a poisoned patient requires an antidote that is not stocked at a particular hospital, the patient must be transferred or the antidote obtained from another hospital. This is complicated by the fact that Canada has lower population density and longer transport distances than the US. In addition, rugged terrain and inclement weather can aggravate transport problems and prolong treatment delays. Consequently, non-availability of essential antidotes may be a greater concern in Canadian hospitals.[8,9] We chose to exclude outpost hospitals and small diagnostics and treatment centres in BC from our survey because they typically do not treat poisoned patients but rely on larger nearby centres to transfer these patients. The fact that these smaller centres do rely on larger hospitals to manage these patients makes having essential antidotes and appropriate quantities even more important in referral centres.

Why is antidote stocking inadequate?

The two greatest barriers to adequate antidote stocking are probably a lack of awareness of the deficiencies and a belief that maintaining such stocks would be excessively costly.[10,11] Prior to 2000, there were no concise, evidence-based guidelines for stocking of emergency antidotes.[2] In the absence of such guidelines, physicians and pharmacists may not know which antidotes need to be stocked. They may conclude, for example, that a rarely used antidote is not worth stocking, or they may be unaware of the need for timely administration of certain antidotes and assume they can obtain these from other facilities in the area at the time they are necessary.[6] In addition, centres that do not perform regular stocking reviews may be unaware of their actual antidote stocks. During the study period there was a manufacturing shortage of glucagon and rattlesnake antivenin, and such shortages occasionally cause shortfalls of specific antidotes. Although stocking shortages may occur for any of the reasons cited, our survey did not solicit explanations for antidote shortfalls; therefore, we cannot determine why BC hospitals understock essential antidotes.

Like previous authors, we found a direct correlation between hospital size and adequacy of stocking. There are several possible explanations. Smaller centres are more likely to lack the personnel and resources to conduct regular stocking reviews. The total acquisition cost for the 14 antidotes included in our study is Can$11 390, and antidote costs probably constitute a larger portion of the pharmaceutical budget in small institutions.[10] To save money, smaller hospitals may choose not to stock antidotes that are expensive or those that expire frequently. Smaller hospitals also tend to be non-teaching hospitals that see fewer severely poisoned patients. They may, therefore, be unaware of stocking requirements.

Solutions

Ideally, every acute care facility in BC should maintain adequate stocks of all the essential antidotes; however, economic realities may make this impossible. In addition, not all hospitals require all of the antidotes deemed essential by the US consensus guidelines and antidote stocking must be tailored to meet local needs. There is no simple, universal solution to the antidote-stocking problem, but there are many partial solutions. Smaller centres may be saved the expense of replacing expired essential antidotes by a system of rotating stock nearing the expiry date to larger centres where it is more likely to be used. Restocking costs are

Table 4. Stocking adequacy by agent (*N* = 75 hospitals)

	No. (and %) of hospitals with adequate stocks							
Antidote	Total	Rural	Urban	Isolated	Non-isolated	Small	Medium	Large
Sodium bicarbonate	58 (77)	26 (60)	32 (100)	9 (69)	49 (79)	21 (55)	27 (100)	10 (100)
N-acetylcysteine	48 (64)	22 (51)	26 (81)	8 (61)	40 (64)	17 (45)	22 (81)	9 (90)
Ethanol	37 (49)	16 (37)	21 (66)	2 (15)	35 (56)	14 (37)	16 (59)	7 (70)
Naloxone	35 (47)	12 (28)	23 (72)	4 (31)	31 (50)	9 (24)	17 (63)	9 (90)
Calcium gluconate	24 (32)	5 (12)	19 (59)	2 (15)	22 (35)	5 (13)	12 (44)	7 (70)
Methylene blue	23 (31)	5 (12)	18 (56)	0 (0)	23 (37)	5 (13)	11 (41)	7 (70)
Atropine	22 (29)	7 (16)	15 (47)	2 (15)	20 (32)	3 (8)	14 (52)	5 (50)
Dimercaprol	20 (27)	6 (14)	14 (44)	3 (23)	17 (27)	5 (13)	9 (33)	6 (60)
Deferoxamine	15 (20)	4 (9)	11 (34)	1 (8)	14 (22)	2 (5)	9 (33)	4 (40)
Cyanide kit	13 (17)	1 (2)	12 (37)	1 (8)	12 (19)	1 (3)	9 (33)	3 (30)
Crotalid antivenin	10 (13)	4 (9)	6 (19)	0 (0)	10 (16)	4 (10)	2 (7)	4 (40)
Glucagon	5 (7)	2 (5)	3 (9)	1 (8)	4 (6)	1 (3)	2 (7)	2 (20)
Pyridoxine	5 (7)	2 (5)	3 (9)	0 (0)	5 (8)	2 (5)	2 (7)	1 (10)
Digoxin F_{ab}	4 (5)	0 (0)	4 (12)	0 (0)	4 (6)	0 (0)	1 (4)	3 (30)

reduced when manufacturers replace unused but expired stock at no cost. Another innovative solution is to develop a sharing system whereby expensive, rarely used antidotes are stored in central locations that are rapidly accessible to more than one facility. British Columbia currently has such a program for digoxin immune F_{ab} fragments and is developing a similar program for fomepizole. The program for digoxin immune F_{ab} fragments, developed by the BC Drug and Poison Information Centre, proved that coordinated antidote distribution can reduce stocking costs and maximize the rational use of costly antidotes.[12] Since inception of this program in 1991, inventory costs were reduced by Can$600 000, and in 242 cases of digitalis glycoside poisoning, an average of 1 vial per patient was saved.

Limitations

One potential problem is that our study data were self-reported and we had no way to confirm its accuracy. Another potential concern is the prolonged time frame during which we accepted responses. The survey was initially distributed late in 1998, but data collection continued until December 2000. Trends in stocking may change from year to year, especially with publication of local, regional, provincial, national or general guidelines, and with the increasing acceptance of new antidotes. Finally, our study included all provincially administered acute care facilities in BC, including those without an emergency department (ED). Since the published guidelines are designed for hospitals with EDs, it could be argued that our study overestimates BC's problem with antidote stocking. On the other hand, we feel that when there is only one hospital in a region, it should be prepared to manage the initial care of a poisoned patient even if it does not have an ED.

Conclusions

This study reveals the inadequacy of antidote stocking in British Columbia. The deficiencies identified in this survey might be corrected by the implementation of provincial stocking guidelines and coordination of antidote purchasing and stocking. This survey represents the first stage in the eventual development of provincial antidote stocking guidelines to correct the understocking of essential antidotes in health care facilities in British Columbia.

Competing interests: None declared.

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