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The Availability of Antidotes in Public Hospitals in Kuwait: A Cross Sectional Survey

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Abstract

Objective: Inadequate availability of essential antidotes is reported in many countries. Information on the availability of antidotes in Kuwait is not available. The aim is to determine whether there are adequate stocks of antidotes in public hospitals in Kuwait and to identify the presence of guidelines for antidote stocking and sharing and to determine the presence of emergency medicine pharmacists in the emergency departments.

Methods: A cross-sectional study was carried out using a questionnaire distributed to chief pharmacists of six public hospitals in Kuwait. The questionnaire enquired on the availability of 29 antidotes.

Results: All the chief pharmacists responded to the survey. The antidotes that were not available in any of the hospitals were botulinum antitoxin, calcium gluconate gel, dicobaltedetate, fomepizole, sodium calcium edetate, sodium thiosulphate, succimer and unithiol. There was substantial variation in the availability of antidotes, especially for cyanide poisoning, ranging from no hospitals for sodium thiosulphate to one hospital each for sodium nitrite and hydroxocobalamin. Only two hospitals had stocks of the polyvalent snake antivenom. Only three hospitals had sharing agreements. Kuwait does not have guidelines for stocking antidotes. None of the hospitals had emergency medicine pharmacists.

Conclusion: The six general hospitals in Kuwait have inadequate availability of certain antidotes. Urgent measures, by creating a national guideline for antidote stocking and enforcing antidote hazard vulnerability assessment and establishing a poison control centre, are needed to reduce morbidity and mortality of poisoned patients in Kuwait.

Keywords: Antidotes; Pharmacist; Kuwait

Introduction

Poisoned patients are managed by supportive measures and/or by the use of specific antidotes. Antidotes can offer significant advantages over supportive measures alone in many poisoned patients. The term 'antidote' is used to refer to any agent used to chelate the toxin, enhance its elimination, neutralize its effect, or ameliorate future complications, rather than just a pure pharmacological antagonist [1]. Antidotes are lifesaving, for example following digoxin or cyanide poisoning and must be available at the appropriate time to be effective.However, it has been reported globally that there is insufficient local availability of essential antidotes, which is of concern as poisoning with certain agents is associated with severe morbidity and mortality [2-8].

In the absence of appropriate guidelines for antidote stocking, recommendations were published for adequate stocking of antidotes in the hospitals of the United States (US) and United Kingdom (UK) [3,9]. It is recommended that hospitals should carry out Hazard Vulnerability Assessment (HVA) for proper stocking of antidotes [3]. Despite the publication of guidelines, a national audit of the acute hospitals in UK revealed that there was significant variation in antidote stocking and that some antidotes for treating poisoning with digoxin, cyanide and toxic alcohols were often not stocked [2].

Kuwait is an Arab country located in the Middle East with a population of approximately 3.9 million people of which, 1.2 million are citizens and 2.7 million are expatriates. Kuwait's healthcare system consists of the private and public sector with the government/public sector consisting of three levels, which are the polyclinics (primary care), six main government/general hospitals (secondary care) and specialized hospitals and clinics (tertiary care). The Central Medical Stores (CMS) in Kuwait is involved in the ordering, stocking and distribution of medications, including antidotes, to hospitals and polyclinics. These public institutions are governed by Ministry of Health (MOH), Kuwait. Usually, the hospitals in Kuwait obtain the required quantities of antidotes from CMS based on the number of poisoned cases admitted. If the CMS doesnot have the needed antidote, it will contact the Health Office Department in Kuwait that contacts its offices in the US and UK. It usually takes a week to one month for the antidote to be available in Kuwait.

According to the official records of the MOH, Kuwait, the annual mean number of poisoning cases was 1005 for the period 1999-2011 [10]. A retrospective survey of all pediatric poisoning cases at the six general hospitals in Kuwait, in 2004 and 2005, showed that a total of 978 children were admitted due to poisoning, which represented 1.8% and 1.6% of all pediatric admissions respectively [11].

The goal of this study is to determine whether antidotes are stocked properly in public hospitals in Kuwait, by comparing with the list of essential antidotes used in the UK audit, as there is no published information on antidote stocking in Kuwait. This study also aims to identify the presence of any national guidelines for antidote stocking andsharing agreements for antidotes between hospitals and to determine

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the presence of Emergency Medicine Pharmacist (EMP) in any of the hospitals surveyed. The results of this study would be beneficial for creating awareness among primary care health professionals and the Kuwaiti government on the need for adequate stocks of antidotes by creating a national guideline for antidote stocking and enforcing antidote HVA in all hospitals and establishing a Poison Control Center (PCC) to monitor the use and distribution of antidotes [12].

Materials and Methods

This cross-sectional survey was approved by the Research Unit, Faculty of Medicine, Kuwait University and the ethical approval was granted by the Ethics Committee, MOH, Kuwait.

The survey was carried out in November 2012 by distributing the questionnaire with the consent form to the chief pharmacists of the six government general hospitals (Jahra, Mubarak Al-Kabeer, Farwaniya, Amiri, Adan and Sabah) personally by one of the authors of this study. The chief pharmacists were selected for this study as they were considered to be the most appropriate persons who were aware of the types and quantities of antidotes stocked in the hospitals.

The questionnaire is an adapted version of the one used in the UK national audit, [2] and permission was obtained from the author. The questionnaire enquired on the quantities and availability of 29 antidotes of which 28 had been recommended in the 2008 College of Emergency Medicine/National Poisons Information Service (CEM/NPIS) antidote guidelines. Intralipid was added to the list by the authors of the UK national audit, as it is recommended for patients severely poisoned with local anesthetics and lipid-soluble drugs [2]. The antidotes were categorized as A (having 12 antidotes for immediate availability in the Emergency Department (ED) or any area where poisoned patients are initially treated i.e. within the hospital), B (13 antidotes within one hour) and C (four for supra-regional stocking). Sections were added to the questionnaire to enquire on the presence of guidelines for antidote stocking, sharing agreements between hospitals, employment of EMPs in ED and whether HVA was done by the hospital.

It was expected that each of the chief pharmacists would complete the questionnaire and return it to the author,who went on a second visit to collect it. A reminder for the non-respondents to complete the questionnaire was done either by phone or email.The survey was completed by March, 2013 and the completed questionnaires were included in the analysis. Descriptive analysis was done using SPSS version 17.

Results

All of the chief pharmacists responded to the survey (100% response rate).

a) Availability of category A antidotes: Antidotes of category A such as acetylcysteine, activated charcoal, intralipid, glucagon, methylene blue, naloxone and flumazenil were available in all hospitals as shown in table 1. The availability of cyanide antidotes was much lower, ranging from no hospitals for sodium thiosulphate and dicobaltedetate to one hospital each for sodium nitrite and hydroxocobalamin. None of the hospitals had calcium gluconate gel. One hospital reported having intralipid available within 1 hour and not immediately.

b) Availability of category B antidotes: There was inconsistent availability of category B list of antidotes as most of the antidotes were available for immediate use and a few were available within one hour in four hospitals (Table 2). Digoxin-specific antibody fragments were stocked as category A instead of the recommended category B.

Table 1: Availability of category A antidotes in the six general hospitals of Kuwait.

Antidote	Indications	Number of hospitals holding the antidote	A[a]	B[a]	C[a]
Acetylcysteine	Paracetamol	6	6		
Activated charcoal	Many oral poisons	6	6		
Calcium gluconate gel	Hydrofluoric acid	None			
Dicobaltedetate	Cyanide	None			
Flumazenil	Benzodiazepines	6	6		
Glucagon	Beta blockers	6	6		
Hydroxocobalamin	Cyanide	1	1		
Intralipid	Local anesthetics	6	5	1	
Methylthioninium chloride (methylene blue)	Methaemoglobinemia	6	6		
Naloxone	Opioids	6	6		
Sodium nitrite	Cyanide	1	1		
Sodium thiosulphate	Cyanide	None			

[a] Number of hospitals stocking the antidotes as: A- immediate availability; B- available within one hour; C- supra-regional

Table 2: Availability of category B antidotes in the six general hospitals of Kuwait.

Antidote	Indications	Number of hospitals holding the antidote*	A[a]	B[a]	C[a]
Calcium folinate	Methotrexate	4	3		
Cyproheptadine	Serotonin syndrome	1	1		
Dantrolene	Neuroleptic malignant syndrome	3	3		
Desferrioxamine	Iron	5	5		
Digoxin-specific antibody fragments	Digoxin	6	5	1	
Ethanol (oral)	Ethylene glycol, methanol	4	4		
Ethanol (intravenous)	Ethylene glycol, methanol	5	4		
Fomepizole	Ethylene glycol, methanol	None			
Octreotide	Sulphonylureas	5	4	1	
Phytomenadione (iv) (vitamin K)	Anticoagulants	6	5	1	
Polyethylene glycol	Gut decontamination: Iron, lithium	4	2	2	
Pralidoxime	Organophosphate insecticide	5	4		
Viper venom antiserum, European	European adder snake bite	None			

*The total numbers for some hospitals are unequal with the numbers added from each category due to missing data.
[a]Number of hospitals stocking the antidotes as: A- immediate availability; B- available within one hour; C- supra-regional

Fomepizole and antivenom for European adder snake bite were not available.

c) Availability of category C antidotes: Antidotes of category C were not available as shown in table 3.

d) Sharing agreements: Only three hospitals had agreements to share antidotes between hospitals.

e) Availability of EMPs: None of the hospitals had EMPs.

Table 3: Availability of category C antidotes in the six general hospitals of Kuwait.

Antidote	Indications	Number of hospitals holding the antidote
Botulinum antitoxin	Botulism	None
Sodium calcium edetate	Lead	None
Succimer	Heavy metal poisoning	None
Unithiol	Heavy metal poisoning	None

f) HVA assessment: None of the hospitals carried out antidote HVA for antidote stocking.

g) Reason for inadequate stocking: Two responders stated that infrequent use was the reason for not stocking some antidotes.

h) Quantities: The quantities of antidotes were not properly reported by the respondents as instructed and there was insufficient information on strength or dosage forms. Therefore, the reported quantities were not analyzed.

Discussion

Our survey of the six general hospitals in Kuwait revealed that there is variation in the availability of antidotes. Dantrolene was stocked in half of the hospitals and none of them had viper venom antiserum. Only one hospital stocked cyproheptadine. Of the 29 antidotes evaluated, nine antidotes were not available in any of the hospitals. There was inadequate stocking of antidotes for cyanide poisoning. A few respondents cited infrequent use as the reason for inadequate stocking of some antidotes. The antidotes in the hospitals in Kuwait were not categorized as A, B or C, as it is commonly perceived that all antidotes should be available at all times in the pharmacy and ED.

Previous studies in other countries had reported that antidotes were inadequately stocked. An Iranian study reported "defective" stocking of antidotes and stated that lack of information regarding access to antidotes and high cost as reasons for this observation [6]. The authors of a prospective observational study of 20 hospitals in the Emirate of Abu Dhabi found that only 2(10%) hospitals had adequate stock of antidotes. Diazepam, sodium bicarbonate and atropine were some of the antidotes that were included in their survey list of 12 antidotes [4]. A cross-sectional survey of 11 hospitals in Palestine, in 2006, found that certain antidotes such as digoxin-specific antibody fragments, folic acid injection and ethanol were not available. None of the hospitals had adequate stock of all the 37 antidotes listed in the survey questionnaire. Some of the reasons for inadequate stocking cited by the authors were lack of awareness of the inadequate availability and the misconception that maintenance of stocks is expensive. They recommend new legislations for antidote stocking and more coordination between local PCC and local hospitals [5]. A study in the US reported that only 1 (0.9%) of the 108 hospitals surveyed had stocked all 8 listed antidotes in adequate amounts. Using a multiple regression analysis they found that the two independent predictors of the number of antidotes stocked inadequately were lack of a formal review of antidote stocking and smaller hospital size [13].

In our study there were only two hospitals which stocked hydroxocobalamin and sodium nitrite as antidotes for cyanide poisoning. As cyanide is a frequent co-intoxication in people who are victims of smoke inhalation and is an extremely dangerous poison, it is recommended that it is essential to have adequate stocks of antidotes for cyanide poisoning. However, it is difficult to determine if suitable cyanide antidotes are stocked in appropriate quantities as experts differ in their opinion over which is more effective and safe [14]. The 2009 expert consensus guidelines recommends to stock two kits of hydroxocobalamin or one cyanide antidote kit (sodium nitrite and sodium thiosulphate)for a 100kg patient [3]. Hydroxocobalamin may be considered as the cyanide antidote of choice because of its safety for widespread use, ease of use and its wider use as for cases of smoke inhalation [14]. However, dicobaltedetate is considered by CEM/NPIS as the antidote of choice for severe confirmed cyanide poisoning [9].

Only three hospitals in our study reported having sharing agreements for antidotes with other hospitals in Kuwait. But an expert panel of the US consensus guidelines has pointed out that there are often delays during the transfer of antidotes from one hospital to another, even "between neighboring hospitals or hospitals under the same management", which can compromise patient care [3]. For example, for a patient with serious digoxin toxicity, a delay of 30 minutes could be fatal.Some of the reasons for delays cited by the expert panel are the lack of a dedicated system for transfer, the unplanned and infrequent nature of transfer requests and difficulties in prioritizing delivery of antidotes to another hospital over other urgent internal orders of the hospital [3].

In our study, none of the hospitals had stocked venom antiserum for the bite of a European adder snake as it is not a common snake in Kuwait. According to the World Health Organization (WHO), the two snakes found in Kuwait are the Arabian horned viper and Morgan's desert cobra, the bites of which require the recommended polyvalent snake antivenom and bivalent Naja/Walterinnesia snake antivenom respectively. These antivenoms are manufactured by the National Antivenom and Vaccine Production Center in Saudi Arabia [15]. Only two hospitals in Kuwait had stocks of the polyvalent snake antivenom. We recommend the antivenom to be available in all hospitals that provide emergency care.

Kuwait does not have a national guideline for antidote stocking. The establishment of a national guideline would enable the availability of antidotes that is suitable to meet the local needs. However, if a "rigid" stocking is recommended for all hospitals, it may lead to insufficient stocking [3]. Therefore, an expert panel of the US consensus guidelines recommended customization of antidote stocking for each hospital by developing the concept of an antidote HVA, which is an adaptation of the HVA required in US by The Joint Commission for Accreditation of Hospitals [3]. In our study, none of the surveyed hospitals had any formal systematic assessments done similar to the recommended antidote HVA but it can be assumed that the antidotes were stocked on the basis of the poisoning presentations to the EDs, although further investigations are required to corroborate this. It is recommended that all hospitals should perform an antidote HVA as there are a variety of variables that may affect institutional antidote requirements such as specialty, size, geographical location, availability of antidotes at neighboring facilities etc. This concept of HVA requires each hospital to assess the need and quantity of each antidote and find the treatment period for which antidote stocking should occur. They also recommend regiona lPCC in the assessment process [3]. In Taiwan, a survey of facilities handling cyanide was conducted to determine the adequacy of their response to a chemical disaster with regard to the availability of a cyanide antidote kit in the facilities and nearby hospitals. Only 10(9.3%) of the 107 facilities had cyanide antidote and of the 38 hospitals, to which a person exposed to cyanide would be referred to by these facilities, only 4 stocked the cyanide antidote. The authors stated that the failure of having the antidotes available would result in considerable morbidity and mortality in the event of a chemical disaster

[7].The NPIS/CEM guidelines of the UK have recommended minimum stocking levels which are based on the quantity of antidote needed to initiate treatment for an adult patient and to continue treatment for the first 24 hours. Hospitals may require higher stock levels and individual departments should determine the quantity of each antidote that they need to stock based on the epidemiology of poisoning presentations to their respective departments [9].

The development of national guidelines for proper stocking of antidotes in Kuwait and measures to achieve compliance with these guidelines is urgently required. However, having published national guidelines is not the only solution for adequate stocking. A study carried out a survey on the availability of antidotes in acute hospitals to determine whether the NPIS/CEM 2008 guidelines for stocking antidotes in EDs in UK had any impact. They received responses from 196 hospitals and found much lower availability of cyanide antidotes ranging from 21% to 74% for hydroxocobalamin and dicobaltedetate respectively. Although intralipid was excluded in the 2008 guidelines, it was available for immediate use in 62% of hospitals. Their survey questionnaire had a list of 29 antidotes. There was suboptimal availability within 1 hour, of antidotes for the treatment of poisoning with glycol and alcohol. The authors observed that despite the presence of national guidelines, there was little improvement in antidote stocking and there were no studies exploring the reasons for inadequate stocking in UK [2]. In Canada, the findings were similar following the introduction of guidelines. Canadian studies have found that high costs and limited awareness as factors contributing to inadequate stocking [16,17].

Most of the respondents in our study did not report the quantities correctly and relevant data such as dosage forms and strengths were missing. Further research on the quantities stocked is required in the future.

Kuwait does not have a PCC. The past century has seen the development and evolution of PCCs worldwide to decrease morbidity and mortality associated with poisons. Several studies have shown that PCCs are cost effective by reducing the number of ED visits, decreasing the length of hospital stay and improving patient outcomes [18] and a play a vital role in monitoring and ensuring safe use and distribution of antidotes [12]. The WHO has stated that a central depot of antidotes could be effective and economically viable to ensure proper distribution of antidotes. A PCC or a central hospital pharmacy would be the most appropriate and logical location for a central depot of antidotes [12]. In Kuwait, the CMS is the central depot of antidotes. However, a PCC has to be established for better monitoring and distribution of antidotes.

In recent years, there is a dramatic increase in the number of EMPs as a result of factors such as changes in the medication management standards of accrediting and regulatory agencies, increased focus on prevention of medication errors in the ED and the role of EMPs in prevention of errors [19]. Research has also indicated that the services provided by pharmacists are highly valued by ED healthcare providers [20]. According to the American Society of Health-System Pharmacists (ASHP), one of the essential direct patient care roles of EMPs involves "the selection and administration of specific antidotes and other supportive therapies" [19]. They may also assist in the preparation of antidotes and provide recommendations for monitoring of safety and effectiveness of antidotes. Collaboration with toxicologists and PCCs is required when these services are provided. The EMPs can play a pivotal role in ensuring adequate stock of antidotes [19]. Considering the benefits of employing an EMP, we recommend their employment in Kuwait for all institutions that provide emergency care.

Our study had several limitations. The analysis of the cost of procurement or storage of antidotes was not done, which may have an influence on the stocking. We were also unable to obtain reliable data on the quantities of antidotes stocked and utilized. This study relied on self-reported data which could not have been verified at the actual site of storage like the pharmacies or EDs and there might have been a social desirability bias which could have led some respondents to overstate the availability of antidotes. We hope to overcome these limitations with further studies in the future focusing on several aspects such as antidote usage patterns in both public and private hospitals, quantities, HVA, factors influencing stocking such as frequency of use, acquisition costs, geographical location, ED case volume, supply chain issues, etc.

Conclusion

The results of this study clearly show that some of the general hospitals in Kuwait have inadequate availability of certain antidotes and none of them have done an antidote HVA. There are no national guidelines and standardized sharing agreements between the hospitals. There are no EMPs in any of the hospitals surveyed. The concerned authorities in Kuwait need to urgently implement measures, such as carrying out antidote HVA for every acute hospital and establishing a PCC and national guidelines to ensure adequate availability of antidotes to reduce morbidity and mortality of poisoned patients.

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