

Evaluation of the availability of antidote for emergency treatment of poisonings in Taif hospitals.

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Abstract

The availability of antidotes are essential and lifesaving in the management of certain poisonings. The purpose of this study was to determine the availability of antidote stocking in hospitals, based on published guidelines for antidote stocking, and to evaluate the impact of hospital types on the availability of antidotes for the management of acute toxic exposures and poisonings in Taif city. Questionnaire (on the availability of antidotes) was sent to all hospitals and emergency departments in Taif city. Collected data were analyzed in SPSS version 17 using descriptive and comparative analysis. Response rate was 75%, there was great variability in the availability of antidotes between hospitals. The availabilities of most antidotes were far better in the military hospitals compared to general hospitals. Most Taif hospitals stocked some important antidotes. Coordination between Saudi hospitals and the Poison Centers is also important.

Keywords: Antidote, availability, hospitals, Taif, poisoning, treatment.

Abbreviation

WHO: World Health Organization, KSA: Kingdom of Saudi Arabia,
TCAs :tricyclic antidepressants, MAOIs: monoamine oxidase inhibitors,
MTX: Methotrexate, NMS: Neuroleptic malignant syndrome, BAL: dimercaprol,
EDTA: Ethylenediaminetetraacetic acid

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INTRODUCTION

Antidotes can be used to reverse the pharmacological effects of a particular poison, to displace a poison from its target organ receptor site, or to deactivate the poison by binding irreversibly to affected molecules. Not all toxic substances have antidotes, thus making the use of such technique as specific treatment. [2] Some patients can recover fully without the use of antidotes. [1] If an antidote is required, its administration should be carried out as early as possible. [3]

In certain circumstances, specific antidotes may significantly reduce the requirement of medical interventions. In addition, they can reduce morbidity, mortality, and the length of hospitalization. This is particularly necessary in countries in which high rates of poisonings exist. In these situations, antidotes may be considered essential and life-saving. [4]

Over the past 25 years, many studies have demonstrated that antidotes are essential and until now they are insufficiently stocked in health care facilities. [5–18] The exact causes of this problem are unknown but appear to be associated with limited hospital resources, cost and possible unfamiliarity with antidotes. Several regional poison control centers in the United States and some textbooks have developed recommendation lists for antidote stocking. [10,19,20].

In 2000, the first evidence-based agreement guidelines for stocking antidotes in the United States were published. These guidelines recommended that 16 essential antidotes should be stocked in each health care facility that treats acutely poisoned patients. [10] Antidotes were considered essential if they were both effective and necessary within the first hour of patient presentation. The quantity of antidote recommended was based on the dose necessary to treat one or two 70-kg acutely poisoned patients for the first 4 hours after exposure. [10,19]

The World Health Organization guidelines for antidotes and their availability have divided antidotes into those that should be immediately available in the emergency department and those that should be available in the hospital for use as symptomatic treatment of poisoning. [20]

There has been no study addressing antidote availability in Taif hospitals. Since poisoning remains a serious problem in Saudi hospitals and various antidotes are frequently under stocked, we initiated a countrywide survey to describe the current antidote availability and anticipated requirements in Saudi hospitals. The purpose of this study was to determine the availability of antidotes at Taif hospitals. The availability of antidotes in each hospital was compared to the 16 antidotes considered essential in the guidelines of stocking antidotes Dart et al. [10]

This is an attempt to encourage the finding of appropriate antidote storage and sharing network in this country. The survey results allow us to communicate with the health administrators in Saudi hospitals to define reasonable budgets for an antidote distribution system.

MATERIALS AND METHODS

Design of study

This is a cross-sectional survey study using a questionnaire that involves descriptive and comparative analysis.

Study area and sample size

The data collection was conducted cover all governmental hospitals in Taif city. A total of 9 hospitals were identified and the addresses and contact information for each one was extracted and recorded. In Taif they are two types of governmental hospitals run by the Ministry of Health and hospitals run by the ministry of defense and aviation, namely the general hospitals and the military hospitals.

Study tool: The questionnaire

A semi-structured questionnaire was developed for the purpose of the current study. A questionnaire was prepared and designed to be self-administered by the heads of the Emergency Departments of each hospital, accompanied by an official document explaining the purpose and importance of the survey. The heads of the Emergency Departments were asked to assign a specialist to complete the questionnaire.

A list of commonly required antidotes and essential drug use in treating poisoning complications was compiled from the WHO and published guidelines for antidotes stocking. [10,20]

The survey

All questionnaires were sent to the 9 hospitals. The hospitals who had not responded were given reminders by telephone calls, another reminder was given 3 months before closing the end of study.

Statistical analysis

Data extracted from the questionnaires was keyed into the Statistical Package for Social Sciences (SPSS version 17) software. Data were analyzed descriptively as frequencies and percentages and comparative analysis.

RESULTS

Responding hospitals and their general Characteristics

Sample size was 12 hospitals, the questionnaire was send to all hospitals. Three hospitals returned the surveys. From the total responses received, three questionnaires were discounted as the hospital returned then without filling with the required information.

Table 1. The availability of each antidotes and essential drugs in military and general hospitals.

Name of hospital	Available	%
1- Alhada hospital	28	68.2%
2- Mansour hospital	21	51.2%
3- Prince Sultan hospital	20	48.7%
4- Abdel Aziz hospital	28	68.2%
5- King Faisal hospital	12	29.2%
6- Children hospital	15	36.5%
7- Chest hospital	7	17.0%
8- Rehab hospital	7	17.0%
9- Psychatric hospital	13	31.7%

Availability of antidotes and essential drugs

Analysis of the collected data, compared to the the guidelines of Dart et al. for stocking 16 emergency antidotes, showed that the availability of specific antidotes ranged from one (fomepizole) to more than 90% atropine sulphate, Phytomenadione (Vitamin K), sodium bicarbonate. However, nine antidotes were severely deficient in most hospitals but available in less than 20% of all hospitals. Those included dimercaprol, polyvalent antivenom, ethanol (100%), pyridoxine, sodium calcium edetate, procyclidine injection, cyproheptadine, calcium folinate and a viper venom antiserum. None of the responding hospitals stocked all of the antidotes on the list.

The top 10 toxic agents most frequently reported by the Accident and Emergency Departments to have been treated at least once during the last year at their hospital. Among the responded hospitals, paracetamol poisoning was in the first rank as it is reported by 86.5% of hospitals, followed by snake bites (82.4%) and bee stings (81.1%). Furthermore, One hospitals reported one case of toxic alcohol exposure, and thus made the alcohol as a toxic agent to be on the tenth ranking place. This result is similar to the data reported by majed et all. [30].

In relation to hospital type, there is great variability in the availability of antidotes (there were significant differences between hospitals for six items). The availabilities of most items are far better in the military hospitals from the general hospitals. calcium gluconate, sodium bicarbonate, atropine sulphate, naloxone, and Flumazenil were available at all military hospitals. Atropine sulphate, sodium bicarbonate and phytomenadione (vitamin K) were available at all general hospitals. (Table 2 and 3).

Availability of other antidotes varied widely from 0% (for Sodium calcium edetate) to 100% (for vitamin K). The availabilities of other antidotes were far better in military hospitals and general hospitals. Vitamin K is available at all general hospitals. By hospital type, the availability of essential drugs varied substantially. Nevertheless, these differences did not reach statistical significance in all cases. Overall, the availability of most of items was excellent, ranging from more than 11% to 100%, except for cyproheptadine and sodium calcium edetate (Table 3).

The response rate of present work was 75.00%, this rate is within the previous ranges reported in studies conducted in accident and emergency department through questionnaires. [24,25] The response rate is higher in this study compared to rates reported in mailed questionnaires for other countries in the Asia Pacific region [12,26].

Results show that a large percentage of antidotes were not available in Taif city hospitals. None of the responding hospitals stocked all of the antidotes on the list, such as calcium gluconate, sodium bicarbonate, atropine sulphate, naloxone, flumazenil and vitamin K which were available at all military hospitals. Atropine sulphate and sodium bicarbonate were available at all general hospitals.

However, seven items were severely deficient in hospitals (available in less than 20% of all hospitals). Those included Polyvalent antivenom, fomepizole, ethanol (100%), pyridoxine, procyclidine injection, calcium folinate and a viper venom antiserum. The antidote cyproheptadine, sodium calcium edetate and dimercaprol was not available in any hospitals.

Since the timely use of antidotes is potentially life saving in certain toxic exposures, maintaining a sufficient stock of antidotes is the responsibility of hospital that provides emergency care. If a poisoned patient needs a certain antidote that is not stocked at a particular hospital, then either the patient must be transferred or the antidote must be acquired from another hospital.

Table 2. Percentage of hospitals stocking the antidotes compared to recommended guidelines for antidote stocking in emergency departments.

Antidote	Indication	Availability %*
1- Atropine sulphate	Bradycardia Organophosphate or carbamate insecticides	100%
2- Calcium gluconate	Calcium channel blockers	77.8%
3- Desferrioxamine	Iron	66.7%
4- Digoxin specific antibody fragments	Digoxin	44.4%
5- Dimercaprol	Arsenic	0%
6- Ethanol	methanol	11.1%
7- Fomepizole	Ethylene glycol	11.1%
8- Glucagon	Beta-adrenoreceptor blockers.	55.6%
9- Methylthioninium chloride (methylene blue)	Methaemoglobinaemia	44.4%
10- N-acetylcysteine	Paracetamol	%55.6
11- Naloxone	Opioids	55.6%
12- Polyvalent antivenom	Significant envenomation	11.1%
13- Pralidoxime chloride	Organophosphate insecticides	55.6%
14- Pyridoxine	Isoniazid	11.1%
15- Sodium bicarbonate	**TCAs, class Ia and Ic antiarrhythmic drugs	100%
16- Cyanide kit	Cyanide	22.2%

** TCAs; tricyclic antidepressants

* The availability of antidotes in each hospital types was compared to the 16 antidotes considered essential in guidelines of Dart et al. for stocking antidotes.[10].

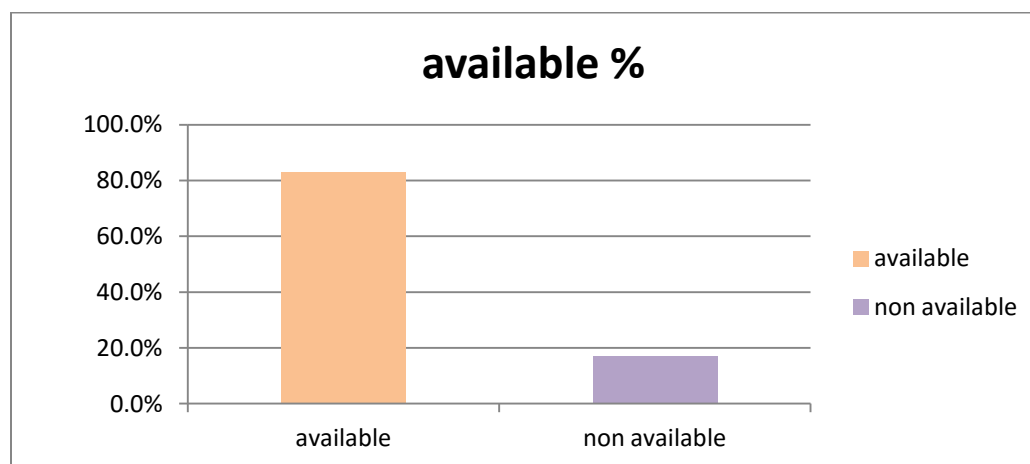


Figure 1. Availability of antidotes in each hospitals.

Table 3. The availability of other antidotes and essential drugs in hospitals.

Antidote	Indication	Availability %
1- Sodium calcium edetate	Heavy metals (particularly lead)	0%
2- Alpha-blocker	epinephrine (adrenaline) Resistant hypertension caused by sympathomimetic drugs of abuse, *MAOIs, clonidine	33.3%
3- Flumazenil	Reversal of iatrogenic over-sedation	88.9%
4- Glyceryltrinitrate or Isosorbide d inirate	Hypertension	77.8%
5- Benzatropine	Acute dystonia	66.7%
6- Protamine sulphate	Heparin	55.6%
7- Phytomenadione (Vitamin K)	Anticoagulants	100%
8- Physostigmine	Anticholinergic toxicity	22.2%
9- Calcium gluconate gel ²	Hydrofluoric acid	22.2%
10- Procyclidine injection	Dystonic reactions	11.1%
11- Cyproheptadine	Serotonin syndrome	0%
12- Calcium folinate	Methotrexate ** (MTX) Methanol, formic acid	11.1%
13- Dantrolene	Neuroleptic malignant syndrome *** (NMS) Other drug-related hyperpyrexia	33.3%
14- Octreotide	Sulphonylureas	44.4%
15- Diazepam or Lorazepam	Convulsions; agitation	88.9%
16- Mesna	Cyclophosphamide	22.2%
17- Penicillamine	Copper, Wilson's disease	22.2%
18- Macrogol '3350' (polyethylene glycol) Klean-Prep®	Gut decontamination for agents not bound by activated charcoal e.g. iron, lithium, bodypackers	22.2%
19- Viper venom antiserum, European	European adder (Vipera berus)	11.1%

* MAOIs: monoamine oxidase inhibitors,

MTX: Methotrexate, *NMS: Neuroleptic malignant syndrome

Alcohol toxicity (ethanol, methanol, and ethylene glycol) has been found to be among the top 10 toxic agents reported by Taif city hospitals. Fomepizole, which is used as an antidote for alcohol toxicity, was not available in eight hospitals in taif city. Ethanol, an alternative antidote, was found to be very scarce among all hospitals (available in <20% of hospitals).

Among hospitals, 86.5% reported paracetamol toxic exposure followed by snake bites in 82.4%. Unfortunately, availability of antidotes used for the treatment of toxic doses of paracetamol and snake bite exposure were less than the actual proportion of hospitals that reported these cases (55.6% for N-acetylcysteine and 11.1% for polyvalent antivenom).

DISCUSSION

A recent Australian study found that the antidote stocked most frequently at sufficient levels was acetylcysteine (68.1%), which is appropriate given the high incidence of paracetamol overdose in Australia [18-27].

Patients with severe cholinergic syndrome from organophosphate poisoning are likely to die from respiratory failure without the early administration of atropine and/or pralidoxime. Interestingly atropine availability was 100% which is higher than the actual proportion of hospitals (67.6%) that reported organophosphate poisoning as has been previously reported [12,16,27].

Antidotes used to treat conditions other than poisonings were more frequently stocked, such as atropine, dopamine, dobutamine, calcium gluconate, diazepam, and sodium bicarbonate. Allergic reactions to bee sting are treated like other allergic reactions. Mild reactions are treated with antihistamines. If a more severe reaction develops, epinephrine should be administered [28].

Among hospitals, epinephrine was available in 33.3%, which has been noticeable to be less to the actual proportion of hospitals (81.1%) that reported bee sting. However, that notice did not confirm whether the hospitals that treated bee sting were the same hospitals that stocked epinephrine. Moreover, since anaphylaxis, delayed allergic reaction and serum sickness have been reported after administration of the antivenom for the snake venom poisoning [19].

Treatment with corticosteroids, H1 blocking agents, and intravenous or subcutaneous epinephrine may be needed if immediate and delayed hypersensitivity reactions occur and should be readily available at the time of antivenom initiation [29].

For knowledge, this is the first publication of antidote stock levels in Taif hospitals (KSA). Our findings are consistent with studies from multiple countries that reported variable and inadequate antidote stocking levels. [5–18] Also, the results obtained were similar to those from developing countries, which suggest that antidote stocking is often inadequate [16,17].

A recent study in South Africa found that seven antidotes were not stocked by any of their hospitals, including digoxin-specific antibody fragments, dimercaprol, calcium disodium edetate, fomepizole, intravenous pyridoxine, silibinin, and succimer.[17] A similar study in north Palestine showed that digoxin-specific Fab antibodies, ethanol, fomepizole, glucagon, penicillamine, physostigmine, succimer, and thiamine were not available at any of the surveyed hospitals.[16]

A recent Australian study designed to determine the stock levels of 13 antidotes in Queensland hospitals showed that no hospital had sufficient stock of all 13 antidotes. The proportion of hospitals with sufficient stocks varied from 0% (pyridoxine) to 68.1% (acetylcysteine). Larger hospitals had a higher frequency of sufficient antidote stocks. Only 16% of hospitals claimed to be able to acquire an antidote from another facility within 30 min. [18] Furthermore, another study in Taiwan revealed inadequate stocking of 20 selected antidotes. The study found that physostigmine, cyanide antidote kit, BAL (dimercaprol), EDTA (calcium disodium edetate), methylene blue, Vipera Russell formosensis antivenin, and botulism antitoxin were not available in most (>90%) hospitals [12].

Bed capacity and number of poisoning cases were the only suggested factors associated with higher antidote stock levels. General hospitals with a larger bed capacity stocked more antidotes, consistent with the findings of previous studies. Also, general hospitals with the highest average number of poisoning cases stocked more antidotes. Another recent study in South Africa found

that tertiary hospitals stock 46% of the antidotes while secondary and private hospitals stock 37% and 35%, respectively [17].

A recent Australian study suggested that possible reasons for availability of antidotes include budget constraints in smaller hospitals, perceived lack of antidote need, short antidote expiry dates, or the assumption that patients or antidotes could be transferred quickly enough if required. However, smaller hospitals can still expect to receive patients with acute poisoning, so a degree of preparedness is required. Decisions regarding the stocking of antidotes are complex from a pharmaco-economic perspective [18].

However, in the Australian study, there was no relationship between antidote cost and the frequency with which it is stocked. For example, atropine is used for treatment of anticholinesterase poisoning and was the cheapest antidote to stock. All hospitals stocked some atropine, but only 27% stocked it sufficient to treat a 70-kg patient [18].

There were some limitations to this study. It is the first of its type. The objective of the study was only to document the availability of antidotes and to evaluate the impact of hospital types on the availability of antidotes for the management of acute toxic exposures and poisonings in Taif hospitals. Other factors that may determine appropriateness of antidote stocking. In addition, this study relied upon self-reported data. No direct observations or location visits were conducted; data collected depended upon knowledge and stock responsiveness of respondents.

CONCLUSION

Most Taif hospitals stocked certain important antidotes. In relation to hospital type, there was great variability in the availability of antidotes. The availabilities of most antidotes were far better in the military hospitals compared to general hospitals. Raising awareness of the importance of antidotes by instruction, regular evaluation of antidote stocking, distribution strategy, and suitable legalization might provide solutions. Coordination between Saudi hospitals and the Poison Centers is also important.

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