REPORT

Availability of antidotes and key emergency drugs in tertiary care hospitals of Punjab and assessment of the knowledge of health care professionals in the management of poisoning cases

Naheed Arslan[1]*, Sonia Khiljee[1], Allah Bakhsh[1], Muhammad Ashraf[2] and Iram Maqsood[1]
[1]Institute of Pharmaceutical Sciences, University of Veterinary & Animal Sciences, Abdul Qadir Jillani Road, Lahore, Pakistan
[2]Department of Pharmacology & Toxicology, University of Veterinary & Animal Sciences, Abdul Qadir Jillani Road, Lahore, Pakistan

Abstract: This study was conducted to evaluate the availability of antidotes / key emergency drugs in tertiary care hospitals of the Punjab province, and to assess the knowledge of health care professionals in the stocking and administration of antidotes in the proper management of poisoning cases. Seventeen (n=17) tertiary care hospitals of Punjab Pakistan were selected. Two performas (A and B) were designed for 26 antidotes / key emergency drugs and given to the hospital pharmacists and physicians respectively. It was observed that Activated Charcoal, being the universal antidote was found only in 6 hospitals (41%). Digoxin Immune Fab, Edentate Calcium disodium and Glucagon were not available in emergency department of any hospital and even not included in the formulary of any hospital. About 80% pharmacists were aware of the method of preparation of Activated Charcoal and 85% physicians were familiar with its route of administration. Data showed that tertiary care hospitals of Punjab do not stock antidotes according to national drug policy. Moreover the study strongly suggests the development of health care centers and professional by organizing antidote awareness programs, continuous education and record keeping of poisonous cases and availability of emergency drugs around the clock.

Keywords: Antidotes, Key Emergency Drugs, Tertiary Care Hospital, ICU (intensive care unit)

INTRODUCTION

WHO reports that poisoning is one of the most common cause of increased morbidity and mortality rate throughout the world (Thundiyil *et al*., 2008). Sedatives, analgesics and antidepressants found to be the most commonly used agents for intentional poisoning in developed or industrialized countries, when used in high doses (McClure, 2001) while pesticides are the major causative agents for self-poisoning or suicidal attempts in Asian countries mostly in rural areas having mortality rate of 10-20% (Marecek, 1998). In America, death rate due to poisoning has increased about six times (from 6,100 to 36,500 cases) in 2008 (Warner *et al*., 2011). Similar study in Karachi also showed that snakebite cases have increased up to 3 times in last five years (Ara, 2012).

Most of the toxicological emergencies do not require the use of antidote and can be treated by gastric lavage and symptomatic treatment only; however specific poisoning cases need the use of specific antidote. Studies showed that well-timed administration of the correct antidote reduces death rate (Gorman *et al*., 2003). The results of multi-center study in USA showed that 80% patients (119 patients out of 150), recovered from digoxin toxicity by timely administration of Digoxin immune Fab (Antman *et al*., 1990). The use of Glycopyrrolate along with antidotes Atropine and Paralidoxime reduced the patient stay in hospitals (Turabi *et al*., 2006). Delayed use or unavailability of antidotes could result in anoxic brain injury or death in cyanide poisoning (Shareef *et al*., 2011). Handling and treatment of snakebite and other poisoning cases, could not be achieved in time due to the lack of awareness about availability of antidotes in hospitals (Mirza *et al*., 2006).

First guidelines for the stocking of *antidotes* were developed by USA in 2000. Individuals/ professionals for the study panel were selected on evidence of previous antidote research or involved in the purchase and use of antidotes. The reference lists of major medical textbooks, and articles formed the basis of evidence-based analysis. It was decided that at least sixteen antidotes must be stocked in emergency department of hospital (Dart, 2000).

A research in Karachi emphasized that improved knowledge and understanding of dog bite management is needed among health professionals, to avoid deaths due to rabies (Salahuddin *et al*., 2011). Only 75% of doctors and 51.1% of nursing staff were aware of the immunization plan against tetanus in children, but the knowledge was found poor for adults (Dabas *et al*., 2005). Only one study is conducted in London to observe the knowledge for specific antidotes (e.g. naloxone, flumazenil,

*Corresponding author: e-mail: naheedarslan@yahoo.com

cyproheptadine and benzodiazepines) used for the treatment of certain recreational drug-induced toxicities. Doctors' knowledge was assessed 68.3% for opioid toxicity and 81% for benzodiazepine toxicity (Lidder *et al*., 2008).

MATERIALS AND METHODS

It is a concurrent survey based study to observe the availability of antidotes and key emergency drugs in tertiary care hospitals of Punjab in Pakistan. The knowledge of health care professionals in tertiary care hospitals of Punjab regarding the dose, route of administration and method of preparation of antidotes and key emergency drugs was also surveyed. Punjab is the biggest and populous province of Pakistan, having various tertiary care hospitals in its different big cities.

Study design

Two performas were designed for this study, one for pharmacists (Performa-A) and the other for physicians (Performa -B). The parameters included in the study, focused three major areas of practice, first to evaluate the availability of 26 antidotes and key emergency drugs, second the knowledge of physicians regarding the dose and route of administration and method of preparation of drugs added in the performa (David *et al*., 2001). In Lahore, survey was done personally, while for other cites information was taken through e-mail and also telephonically. Sample size was n=17 for tertiary care hospital.

For physicians knowledge, 5 large tertiary care hospitals of Lahore were selected, named A, B, C, D and E with accident and emergency departments. Forty physicians were interviewed during the study. Selection was random, on the availability and willingness of physicians to fill the performa. Similarly forty pharmacists from all tertiary care hospitals were asked to provide information regarding the availability of antidotes, if added in formulary, route of administration and method of preparation of drug.

Selection criteria

Physicians working in emergency departments and intensive care units (ICU) of the hospitals were asked to fill the performa, while working in departments like plastic surgery, skin, ortho and outpatient were excluded. The pharmacists working in emergency department, ICUs and pharmacy departments of hospitals were selected.

Statistical design

Data was entered into an Excel 2007 (Microsoft) database and imported to SPSS statistical software (Version 17) for analysis. Standard descriptive statistics were reported including means and standard deviations for the availability of antidotes in hospitals. Simple ratio test was applied for the response of health care professionals about dose, route of administration and method of preparation of mentioned drugs.

RESULTS

Our survey of tertiary care hospitals in the Punjab, Pakistan depicted that only 4 out of 17 hospitals stocked sufficient Desferroxamine antidote required for the initial treatment of even one case of acute iron poisoning, as seen all over the world North Palestine (Sawalha *et al*., 2007), British Colombia (Gorman *et al*., 2003) and Ontario etc. The data showed that tertiary care hospitals had adequately stocked a mean of 10.26±5.75 antidotes out of 26 antidotes / key emergency drugs.

As shown in table 1, Inj. Calcium gluconate, Inj. Sodium bi carbonate and Inj. Atropine sulphate were the only antidotes adequately stocked in all surveyed tertiary care hospitals. Anti Rabies Vaccine and Snake Anti-Venom were available in 70% hospitals. Inj. Flumazenil was available only in the emergency department of 5 hospitals with a ratio of 30%. None of the hospital stocked Digoxin immune fab., Inj. Glucagon and EDTA and none of these drugs were included in the formulary of any hospital. All the three drugs are lifesaving and must be available (Dart *et al*., 2000) and stocked in a quantity required to treat a patient of 70kg for first 24 hour (Dart *et al*., 2009) and for a 100kg patient (BEAM 2006). Digoxin immune Fab.is the first line of treatment for digitalis poisoning (Flanagan and Jones 2004). Just 41% of the hospitals had appropriate supplies of Activated Charcoal.

Adequate stocking of all emergency drugs was observed in the surveyed hospitals except for Tetanus immunoglobulin which was available only in 3 hospitals as shown in table 2. Mortality rate from tetanus had increased up to fifty percent in developing countries like Pakistan (Wasay *et al*. 2008) and a study in tertiary care hospital in Lahore reported 100% mortality among premature neonates with tetanus, and 44% mortality in full term neonates (Shah *et al*. 2007).

Several studies had acknowledged deficiencies in knowledge of doctors about their understanding of doses and route of administration of drugs used in various diseases, However no study on the knowledge of antidotes is conducted in Pakistan or in the world except in Guy's and St Thomas Poisons Unit, where the knowledge and use of Naloxone, Flumazenil, Cyproheptadine and Benzodiazepines that are used for the management of certain recreational drug-induced toxicities (Lidder *et al*., 2008). This survey shows the doctors and pharmacists awareness of the antidotes.

Table 1: Status of antidotes availability in tertiary care hospitals of Punjab Pakistan

Name of the Antidotes	Availability in Hospitals (n=17)	Percentage Availability	Name of the Antidotes	Availability in Hospitals (n=17)	Percentage Availability
Activated Charcoal	7	41.11%	Inj. Desferroxamine 500mg (1ml)	4	23.53%
Inj. Atropine 1mg/ml (1ml)	17	100%	Inj. Nalaxone 0.4mg/ml (1ml)	11	64%
Inj. Calcium Gluconate 10% (10mL)	17	100%	N-acetylcysteine 100/200mg sachet	2	11.76%
Inj. Digoxin Immune Fab 40mg vial	0	100%	Inj. Physostigmine Sulphate1mg/ml	1	6%
Inj. Edetate Calcium disodium 200mg/ml (5ml)	0	0%	Inj. Protamine Sulphate 10mg/ml	2	11.76%
Inj. Flumazenil 0.1mg/ml (10mL)	5	29.41%	Rabies Vacccine 2.5iu/ml (1mL)	12	70.58%
Inj. Glucagon 1mg (1ml)	0	0%	Snake Anti Venom 10ml	12	70.58%
Inj. Pralidoxime HCl 200mg/ml (1g)	6	35.29%	Tab. Pyridoxine 50mg	3	17.64%
Inj. NaHCO3 8.4 %w/v (20ml)	17	100%	Inj. Vitamin K	15	88.23%

Table 2: Status of emergency drugs availability in tertiary care hospitals of Punjab

Name of the Emergency Drugs	Availability in Hospitals (n=17)	Percentage Availability	Name of Emergency Drugs	Availability in Hospitals (n=17)	Percentage Availability
Inj. Magnesium Sulphate 50% (2ml)	12	70.58%	Inj. Calcium Gluconate 10% (10mL)	17	100%
Inj. Adrenaline 1mg/ml (1ml)	17	100%	Inj. Pheniramine maleate 25mg/ml (2ml)	16	94.11%
Inj. Dexamethasone 4mg/ml (1ml)	17	100%	Inj. Sodium bicarbonate 7.5/ 8.4 %w/v, (20ml)	17	100.00%
Inj. Diazepam 5mg/ml (2ml)	16	94.11%	Inj. Octreotide 0.05mg(1ml)	10	58.82%
Inj. Hydrocortisone sodium 500mg	17	100%	Inj. Tetanus Immunoglobulin	3	17.64%

Table 3: Percentage Knowledge of Pharmacists for method of preparation / reconstitution of antidotes

Name of Antidotes	Percentage	Name of Antidotes	Percentage
Activated Charcoal	80%	Inj. Desferroxamine 500mg	0%
Inj. Atropine 1mg/ml (1ml)	90%	Inj. Nalaxone 0.4mg/ml (1ml)	90%
Inj. Calcium Gluconate 10% (10mL)	50%	N-acetyl cysteine 100/200mg sachet	40%
Digoxin Immune Fab 40mg vial	10%	Inj. Physostigmine Sulphate1mg/ml	10%
Edetate Calcium disodium 200mg	0%	Inj. Protamine Sulphate 10mg/ml	20%
Inj. Flumazenil 0.1mg/ml	40%	Rabies Vacccine 2.5iu/ml (1mL)	80%
Inj. Glucagon 1mg (1ml)	0%	Snake Anti Venom 10ml	70%
Inj. PralidoximeHCl	50%	Tab. Pyridoxine 50mg	40%
Inj. NaHCO3 8.4 %w/v (20ml)	70%	Inj. Vitamin K, 10mg/ml	80%

Table 4: Knowledge of Pharmacists regarding the route of drug administration of antidotes

Name of Antidotes	Percentage	Name of Antidotes	Percentage
Activated Charcoal	90%	Inj. Desferroxamine 500mg	25%
Inj. Atropine 1mg/ml (1ml)	85%	Inj. Nalaxone 0.4mg/ml (1ml)	75%
Inj. Calcium Gluconate 10% (10mL)	85%	N-acetyl cysteine 100/200mg sachet	55%
Digoxin Immune Fab 40mg vial	0%	Inj. Physostigmine Sulphate1mg/ml	5%
Edetate Calcium disodium 200mg	0%	Inj. Protamine Sulphate 10mg/ml	30%
Inj. Flumazenil 0.1mg/ml	55%	Rabies Vacccine 2.5iu/ml (1mL)	25%
Inj. Glucagon 1mg (1ml)	5%	Snake Anti Venom 10ml	75%
Inj. Pralidoxime HCl	60%	Tab. Pyridoxine 50mg	30%
Inj. NaHCO3 8.4 %w/v (20ml)	80%	Inj. Vitamin K, 10mg/ml	50%

Table 5: Percentage knowledge of Physicians for the route of antidotes administration

Name of Antidote	Percentage	Name of Antidote	Percentage
Activated Charcoal	85%	Inj. Desferroxamine 500mg	20 %
Inj. Atropine 1mg/ml (1ml)	100 %	Inj. Nalaxone 0.4mg/ml (1ml)	75 %
Inj. Calcium Gluconate 10% (10mL)	95%	N-acetyl cysteine 100/200mg sachet	25 %
Inj. Digoxin Immune Fab 40mg vial	5 %	Inj. Physostigmine Sulphate1mg/ml	0%
Inj. Edetate Calcium disodium 200mg	0%	Inj. Protamine Sulphate 10mg/ml	0%
Inj. Flumazenil 0.1mg/ml (10mL)	65 %	Rabies Vacccine 2.5iu/ml (1mL)	75 %
Inj. Glucagon 1mg (1ml)	0%	Snake Anti Venom 10ml	75 %
Inj. Pralidoxime HCl	25 %	Tab. Pyridoxine 50mg	60 %
Inj. NaHCO3 8.4 % w/v (20ml)	70 %	Inj. Vitamin K 10mg/ml	95 %

Table 6: Physicians Knowledge about Dose of Antidotes

Name of Antidote	Percentage	Name of Antidote	Percentage
Activated Charcoal	60%	Inj. Desferroxamine 500mg	25%
Inj. Atropine 1mg/ml (1ml)	60%	Inj. Nalaxone 0.4mg/ml (1ml)	80%
Calcium Gluconate 10% (10mL)	65%	N-acetyl cysteine 100/200mg sachet	25%
Digoxin Immune Fab 40mg vial	00%	Inj. Physostigmine Sulphate1mg/ml	0%
Edetate Calcium disodium 200mg	5 %	Inj. Protamine Sulphate 10mg/ml	0%
Inj. Flumazenil 0.1mg/ml	55%	Rabies Vacccine 2.5iu/ml (1mL)	65%
Inj. Glucagon 1mg (1ml)	0%	Snake Anti Venom 10ml	75%
Inj. Pralidoxime HCl	40%	Tab. Pyridoxine 50mg	25%
Inj. NaHCO3 8.4 %w/v (20ml)	30%	Inj. Vitamin K 10mg/ml	80%

DISCUSSION

Majority of the pharmacists (80-90%) were aware of the method of preparation / reconstitution of 5 commonly used antidotes namely, atropine, charcoal, naloxone, anti rabies vaccine and Vitamin K, whereas 60-70% knew about sodium bicarbonate and snake anti venom. No one was familiar with the method of preparation of Inj. desferoxamine, inj. Glucagon and EDTA. A very poor (10%) response was observed in case of Digoxin Immune Fab and Protamine Sulphate (table 3).

Majority of pharmacists and doctors (80-90%) had correct knowledge of route of administration of 4 most commonly used antidotes, including atropine, activated charcoal, calcium gluconate and sodium bicarbonate whereas only half were familiar with the route of vitamin K (tables 4 & 5). 60-80% doctors were sure about the rout of above mentioned 5 antidotes while rest were unsure. Less than 30% were aware of correct route of 3 antidotes and the remaining answered as not sure. About 80% of the surveyed doctors were having correct knowledge of dose of vitamin K and nalaxone (table 6). Poor response was observed in for EDTA, digoxin Immune Fab, protamine sulphate and physostigmine for route of administration as well as for dose.

CONCLUSION

It is concluded that hospitals of the Punjab Province do not stock adequate supply of antidotes, whereas availability of emergency drugs was found quite satisfactory. On the other hand, the area of knowledge of health care professionals need to be improved by introduction of continuous education programs, case studies and inventory control by proper record keeping of poisonous cases. It is the need of hour to establish Drug & Poison Information Centre and antidote banks at institutional level in Punjab.

REFERENCES

Antman EM, Wenger TL, Butler VP Jr, Haber E and Smith TW (1990). Treatment of 150 cases of life-threatening digitalis intoxication with digoxin-specific Fab antibody fragments. Final report of a multicenter study. *Circulation*, **81**(6): 1744-1752.

Ara J (2012). Increasing poisoning trend in Pakistan. dawn. com/2012/04/21/poisoning-cases-at-jpmc-trebled-in-five-years/.

Dabas P, Agarwal CM, Kumar R, Taneja DK, Ingle GK and Saha R (2005). Knowledge of general public and health professionals about tetanus immunization. *Indian J. Pediatr.*, **72**(12): 1035-1037.

Dart RC, Goldfrank LR, Chyka PA, Lotzer D, Woolf AD, McNally J, Snodgrass WR, Olson KR, Scharman E, Geller RJ, Spyker D, Kraft M and Lipsy R (2000). Combined evidence-based literature analysis and consensus guidelines for stocking of emergency antidotes in the United States. *Annals of Emergency Medicine*, **36**(2): 126-132.

Gorman SK, Zed PJ, Purssell RA, Brubacher J and Willis GA (2003). Antidote stocking in British Columbia hospitals. *CJEM.*, **5**(1): 12-17.

Joint Commission on Accreditation of Healthcare Organizations (1998). Comprehensive Accreditation Manual for Hospitals. Oakbrook Terrace, IL: Joint Commission on Accreditation of Healthcare Organizations, **1**: 111.

Juurlink DN, McGuigan, MA, Paton TW, Redelmeier and Donald A (2001). Availability of antidotes at acute care hospitals in Ontario. *Canadian Medical Association Journal*, **165**(1): 27.

Lidder S, Ovaska H, Archer JR, Greene SL, Jones AL, Dargan PI and Wood DM (2008). Doctors' knowledge of the appropriate use and route of administration of antidotes in the management of recreational drug toxicity. *Emerg. Med. J.*, **25**(12): 820-823.

Marecek J (1998). Culture, gender and suicidal behavior in Sri Lanka. *Suicide Life Threat Behav.*, **28**: 69-81.

Marraffa JM, Cohen V and Howland MA (2012). Antidotes for toxicological emergencies: A practical review. *Am. J. Health Syst. Pharm.*, **69**(3): 199-212.

McClure GM (2001). Suicide in children and adolescents in England and Wales 1970-1998. *Br. J. Psychiatry*, **178**: 469-474.

Mirza M, Saini D, Dickens MA, Kazzi Z and Orthner HF (2006). A regional database of antidote availability. *AMIA. Annu. Symp. Proc.*, p.1034.

Salahuddin N, Jamali S, Ibraheem K and Sardar S (2011). Awareness about rabies post exposure prophylaxis in Pakistan among patients and health care workers: Results from an Asian rabies expert bureau study. *J. Coll. Physicians. Surg. Pak.*, **21**(8): 491-494.

Shah AA, Ali AS, Hussain RR, Hussain A, Saeed A and Butt TK (2007). Complications and outcome of neonatal tetanus. *Pak. Paed. J.*, **13**: 126-131.

Sawalha AF, Sweileh WM, Zyoud SH and Al-Jabi SW (2007). Antidote stocking at hospitals in north palestine. *OJHAS.*, **5**(4): 1-7.

Sharif Y, Al Dweik R and Al Qawasme K (2011). Availability of poison antidotes in Abu Dhabi hospitals. *Pharmacology.* Online available at: http://www.middleeasthealthmag.com/cgi-bin/index.cgi?http://www.middleeasthealthmag.com/jan2011/feature4.htm

Thundiyil JG, Stober J, Besbelli N and Pronczuk J (2008). Acute pesticide poisoning: A proposed classification tool. *Bull World Health Organ*, **86**: 205-209.

Turabi A, Hasan S, Ara J and Ahmed M (2006). Drug overdose; study conducted at national poison control center. *Pak. Jour. of Pharma. Sci.*, **23**(1): 31-37.

Warner M, Chen LH, Makuc DM, Anderson RN and Minino AM (2011). Drug poisoning deaths in the united states, 1980-2008. National Center for Health Statistics Data Brief. No. 81. Online available at: http://www.cdc.gov/nchs/data/databriefs/db81.htm

Wasay M, Khatri IA and Salahuddin N (2008). Tetanus and rabies eradication in Pakistan: A mission not impossible. *J. Pak. Med. Assoc.*, **58**(4): 158-159.