Bulletin of High Institute of Public Health
Vol. 38 C.1 [2008]

Management of Hazardous Pharmaceutical Waste Generated from Health Care Facilities

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Abstract: According to the United States Environmental Protection Agency (USEPA), a number of drug entities and pharmaceutical formulations, generated in health care facilities, meet the definition of hazardous waste, including epinephrine, warfarin, nicotine, and seven chemotherapeutic agents. This study has been carried out to assess the hazardous pharmaceutical waste generation in one large multi-specialty hospital in Alexandria for the ultimate objective of recommending an environmentally sound management plan for this waste. Alexandria University Main Hospital was selected for the study. A checklist containing the names of the drugs that are considered hazardous upon disposal was developed. Data concerning the generation and the management of this waste were collected using 2 questionnaire forms. The study revealed that ten hazardous pharmaceuticals are generated from the hospital departments. They are Epinephrine, m-cresol, phenol, silver sulfadiazine, multi-mineral formulations containing Cr and Se, warfarin, cyclophosphamide, chlorambucil, melphalan, and daunomycin. These drugs, as well as the other pharmaceutical waste, are managed as infectious waste: collected in yellow bags, stored in the storage area for infectious waste, and transported by the Private Company responsible for solid waste management in Alexandria Governorate to treatment by shredding and autoclaving prior to ultimate landfill. Consequently, the study recommended a hazardous pharmaceutical waste management plan taking into consideration other equally hazardous drugs such as all chemotherapeutic agents, mutagenic or teratogenic substances, endocrine disruptors, and immunosuppressant drugs. Thermal destruction of all these drugs would provide the highest level of best management practice available at this time. The ash resulting has to be tested and eventually disposed in a lined hazardous waste landfill.

Key words:
Pharmaceutical waste; Hazardous waste; Health care facilities; Waste management; Epinephrine; Chemotherapeutic agents

INTRODUCTION

In a health care facility, pharmaceutical waste is generated through a wide variety of activities, including but not limited to intravenous (IV) preparation, spills/breakage, partially used vials, syringes, and IVs, discontinued, or unused preparations, patients' personal medications, and outdated pharmaceuticals.(1)

In Italy, researches have identified a

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group of pharmaceuticals (ofloxacin, furosemide, atenolol, hydrochlorothiazide, carbamazepine, ibuprofen, spiramycin, bezafibrate, erythromycin, lincomycin and clarithromycin) in the aquatic environment and also in samples of ground and drinking water.[2,3]

Another one-year monitoring study was performed to evaluate the occurrence, persistence, and fate of a group of pharmaceuticals of various therapeutic categories (ibuprofen, acetaminophen, dipyrone, diclofenac, carbamazepine and codeine) in a Sewage Treatment Plant (STP) located in the south of Spain. The removal efficiencies of the STP for these compounds varied from 20% (carbamazepine) to 99% (acetaminophen), but in all cases resulted insufficient in order to avoid their presence in treated water and subsequently in the environment.[4]

In Finland, the occurrence of eight pharmaceuticals (β-blockers: acebutolol, atenolol, metoprolol and sotalol; antiepileptic: carbamazepine; fluoroquinolone antibiotics: ciprofloxacin, norfloxacin, ofloxacin) was assessed in the raw and treated sewage of 12 STPs. In the treatment plants, Carbamazepine was not eliminated during the treatment and in fact even higher concentrations were frequently found in the treated than in the raw sewages. The increase in concentration was shown to be most likely due to enzymatic cleavage of the glucuronic conjugate of carbamazepine and release of the parent compound in the treatment plant. The β-blockers were eliminated in average by less than 65%. This work showed that especially carbamazepine and the β-blockers may reach the recipient waters and there is a need to enhance their elimination in the STP. In this attempt, a denitrifying biofilter as a tertiary treatment could be of minor importance since in this study it did not result in further elimination of the target compounds.[5]

Although the significance of

pharmaceuticals as trace environmental pollutants is largely unknown, the pharmaceutical residues in the environment pose two immediate concerns:

First, with respect to ecological integrity, there is a potential for adverse effects on aquatic biota. Pharmaceuticals that are endocrine disruptors, such as the synthetic estrogen commonly used in oral contraceptives, may impact reproduction of aquatic organisms at low concentrations. Several studies have been conducted and indicated that exposure of fish to synthetic estrogen causes reproductive effects such as changes in sperm density, gonad size, reduced viability of eggs, and male sex reversal.[6-8] Concentrations at which these effects were observed were lower than concentrations detected in surface waters sampled.[9]

Second, drug residues that make their way to drinking water sources could pose the potential for significant rise in antibiotic resistance. Ampicillin-resistant bacteria were found in every United States River tested in 1999. In a 2000 study, all samples taken from the Ohio River contained *Escherichia coli* with some resistance to penicillin, tetracycline, and vancomycin. Samples containing the highest levels of antibiotics also contained bacteria with the greatest resistance.[10]

As research data accumulate on the adverse impacts of waste pharmaceuticals on human health and the environment, applying the Precautionary Principle becomes increasingly relevant: “When an activity raises threats of harm to human health or the environment, precautionary measures should be taken even if some cause and effect relationships are not fully established scientifically.”[11]

According to the United States Environmental Protection Agency (USEPA), a number of drug entities and pharmaceutical formulations meet the

definition of hazardous waste, including epinephrine, warfarin, nicotine, and seven chemotherapeutic agents. Following such a definition, these drugs are deemed to be so detrimental to the environment that they must be segregated for special waste management and can not be sewered or landfilled. In addition, many other drugs are also of concern to EPA: They include hormones, antibiotics, antidepressants, antihypertensives, and some potent drugs. They are not caught by the hazardous waste regulations as these regulations have not been updated since their inception in 1976 and as a result have not kept pace with drug development. Best management practices encourage managing these drugs as hazardous waste when discarded.(9)

In Egypt, discharge of drugs to sewerage system does not violate water regulations as drug residues are not covered by regulations for water quality.(12) In addition, law 4/94 that governs hazardous waste management including health care waste does not distinguish hazardous pharmaceutical waste that has to be incinerated, from hospital infectious waste that can be either incinerated or autoclaved.(13)

Accordingly, this study has been carried out to assess the hazardous pharmaceutical waste generation in one large multi-specialty hospital in Alexandria for the ultimate objective of recommending an environmentally sound management plan for this waste.

Objectives of the study:

1. Developing a checklist with the names of the drugs that are considered hazardous upon disposal.
2. Determination of the source of these hazardous pharmaceutical wastes within a multi-specialty hospital.
3. Study of the management of these hazardous pharmaceutical wastes within the surveyed hospital.
4. Recommendation of an

environmentally sound management plan for pharmaceutical waste generated in health care facilities.

MATERIAL AND METHODS

1. Study setting: Alexandria University Main Hospital.
2. The checklist was developed using USEPA guidelines.[1,9,14]
3. Data collection: Two questionnaire forms were designed:

a) The first was directed to each department in the hospital asking about the generation of any drug waste listed among the pre-developed checklist.

b) The second questionnaire was directed to the Head of the Nursing Staff asking about the system adopted for pharmaceutical waste management.

RESULTS AND DISCUSSION

a) Hazardous pharmaceutical waste checklist:

Table 1 presents a list of drugs that are considered hazardous waste upon disposal.[1,9,14,15] Waste may be considered hazardous if it falls under one of the following two categories: (1) listed wastes, which appear on four lists developed by the USEPA (F, K, P, and U lists) and (2) characteristic wastes which exhibit certain hazardous characteristics such as ignitability, corrosiveness, reactivity and toxicity.[16] From Table 1, it is obvious that eight pharmaceuticals are P-listed, 19 are U-listed, 4 are ignitable, and 4 formulations may be considered toxic.

One of the primary criteria for including a drug on the P-list as acutely toxic is an oral lethal dose of 50 mg/kg (LD50) or less. LD50 is the amount of a material, given all at once, which causes the death of 50% of a group of test animals. Furthermore, a container that has held a P-listed waste is not considered empty unless it has been: (1) Triple rinsed, and (2) The rinsate is managed as hazardous waste. Since triple rinsing is not practical in health care settings, all vials, IVs, and other containers

that have held a P-listed drug must be managed as hazardous waste, regardless of whether or not all of the contents have been removed.[1]

Concerning U-listed items, they are considered toxic (e.g., phenol, lindane, and some antineoplastic drugs). A container that has held a U-listed waste is considered empty if (1) All the contents have been removed by normal means, such as drawing liquid out with a syringe; and (2) No more than 3% by weight remains. If both of these criteria are not met, the container must be managed as hazardous waste. In addition, any residues removed from the empty container must be managed as hazardous waste.[9]

Ignitability applies to formulations that have a flash point less than 60°C (e.g., rubbing alcohol, some topical preparations) or that are strong oxidizers such as amyl nitrite. As regards to toxicity, it applies to formulations containing some chemicals or heavy metals that may leach from the landfill environment in concentrations above the regulatory levels set up by the USEPA (e.g., 100 mg/L barium, 1 mg/L cadmium, 1 mg/L selenium, 0.2 mg/L Hg, or 200 mg/L cresol.)[17] A container that has held a characteristic waste (ignitable or toxic) is defined as empty in the same manner as in case of U-listed waste: when all of the contents have been removed through normal means and no more than 3% by weight remains.[1]

b) Generation of hazardous pharmaceutical waste in Alexandria University Main Hospital:

This is a large hospital of 1765 beds, it serves about 295 inpatients/day, and 992 outpatients/day. Trying to cover the different pharmaceutical waste generation activities, the study covered 30 sites within the Hospital. They included 6 special units (Cardiac, burns, poisons, renal dialysis, bone marrow transplantation, and respiratory units), in addition to 3 operation theatres, 3 post-operative (recovery)

rooms, and 3 Intensive Care Units (ICU). The survey also covered 5 pharmacies (one clinical pharmacy serving hematological patients besides 4 ordinary ones serving different departments). The reception area and 9 wards (oncology, leukemia, hemorrhage, gangrene, surgery, internal medicine, injuries, and ophthalmology) were also included in the study sample.

Results of the survey revealed that among the 35 hazardous pharmaceutical wastes stated in Table 1, only 10 are generated in the surveyed Hospital (Table 2). Epinephrine in the form of adrenaline tartarate of 1mg/ml concentration is by far the most common hazardous drug waste generated (generated in 22 sites/30 under study). This was in accordance to Pines E and Smith C, who stated that in health care settings, waste epinephrine is used most often in cardiac care units and during orthopedic and ophthalmic surgical procedures but may be generated anywhere in the facility to treat cardiac arrest and allergic reactions.[1]

Following epinephrine, m-cresol had the second rank (18/30). It is found as preservative in Human Insulin vials. Third, phenol and silver sulfadiazine took place (16/30). Phenol is used as antiseptic for cleansing purposes, and is a preservative in Neostigmine vials as well as in Human Insulin vials. Selenium and Chromium, being ingredients in some multi-mineral formulations, were found to be generated from 15 sites out of the 30 ones under study. They were followed by the anti-coagulant warfarin, and the 4 antineoplastic drugs cyclophosphamide, chlorambucil, melphalan, and finally daunomycin (Figure 1).

As far as the point of generation is concerned, each of the poison unit, the hemorrhage ward, and the reception area was found to generate 6 hazardous pharmaceutical wastes, while an absence of such waste generation was observed in

the dialysis unit (generating iron, erythropoietin, and dexamethasone in IVs) and in the pharmacies owing to the reverse distributor system adopted by the Hospital.

c) Assessment of the management of hazardous pharmaceutical waste within Alexandria University Main Hospital:

Using a pre-designed questionnaire, an interview with the Head of the Nursing Staff revealed the following:

- There are 3 waste streams in the surveyed hospital: infectious waste, sharps, and non-infectious waste
- Generation rate of sharps and infectious waste within the Hospital is 900 Kg/day (Rates on 3 successive days were 840, 820, and 940 Kg/day)
- The Company responsible for solid waste management in Alexandria Governorate is responsible about the collection of the sharps and the infectious waste generated and their treatment by shredding followed by autoclaving.
- In the Hospital under study, pharmaceutical waste is considered as a type of the infectious waste generated. Consequently, it is collected in yellow bags, stored in special red or yellow containers (Figure 2) for less than 24 hours in the storage area specified for infectious hospital waste (Figure 3), and transported by the responsible company (Figure 4) to treatment by autoclaving, and disposal off in a sanitary landfill. This was found to be in accordance to Smith C who stated that medical waste disposal firms in USA offer a waste stream for chemotherapeutic waste. This waste stream is managed as biohazardous infectious waste that is microwaved or autoclaved then shredded and landfilled, although none of these processes ensure the destruction of

the organic molecules and their proper final disposal.[14]

- No special records are kept tracking the generation of pharmaceutical waste (point of generation, names, quantities).
- No pharmaceutical waste is dropped down the sewerage system.
- Pharmacists and nurses in the Hospital are aware about the environmental hazards caused by chemotherapeutic drug waste and immunosuppressant drug waste as the ones that need to be sent to a regulated incinerator. They succeeded in making a fourth waste stream consisting of these drugs in order to send them to the Cement Factory to be incinerated there, but their proposal was refused from the Factory.

d) Hazardous pharmaceutical waste management plan:

1. An interdepartmental, multidisciplinary team should be formed in the hospital to be accountable for the management of pharmaceutical waste.
2. A comprehensive drug inventory has to be performed in order to determine which ones must be managed as hazardous waste (Referring to Table 1).
3. Best management practices encourage managing some other drugs as hazardous waste when discarded:

- All Chemotherapeutic Agents: Only 9 chemotherapeutic drugs are listed as hazardous. These were the drugs in use till 1976. Over 100 equally hazardous drugs currently in use today are not identified as hazardous. For example: methotrexate, vinblastine, 5-fluorouracil, etc.
- Drugs with LD50s less than or equal to 50 mg/kg
- Drugs meeting National Institute for Occupational Safety and Health (NIOSH) or Occupational Safety and Health Administration (OSHA) criteria.

Such criteria include mutagenicity, carcinogenicity, teratogenicity, genotoxicity, or reproductive toxicity.

- Endocrine Disruptors (e.g., contraceptives, oxytocics)
- Immuno-suppressants.
- Vitamin and mineral preparations with potential toxicity due to their content of chromium, selenium, or cadmium.(1)

4. Once the pharmaceuticals have been classified as to their hazardous waste status, the next challenge is to choose a method for communicating that information to pharmacy and nursing staff as they generate pharmaceutical waste during the course of their everyday activities. A sticker can be placed on the drugs upon their arrival in the pharmacy. The pharmacist either can consult a list to determine the appropriate sticker or use reference shelf stickers, which is preferable to save time and avoid errors.
5. Policies for hazardous pharmaceutical waste minimization should be addressed: it is important to ask what pharmaceuticals are being wasted, and why they are being wasted. Waste minimization can be performed for example by considering lifecycle impacts in the purchasing process (far expiry date, products with no preservative, less packaging, etc)
6. Following waste minimization, hazardous pharmaceutical waste generated should be segregated for special handling. Ideally, segregation should be at the point of generation and waste should be discarded in hazardous pharmaceutical waste containers that are located as conveniently as practical to the point of generation. Personnel that are trained to handle hazardous waste transfer the containers from the point of generation to the central storage area where they

are picked up by a permitted hazardous waste broker.

Conclusion:

1. Researches have identified a group of pharmaceuticals as trace pollutants in the aquatic environment.
2. About 35 pharmaceuticals generated in hospitals meet the USEPA definition of hazardous waste.
3. In Alexandria University Main Hospital, 10 pharmaceuticals are considered hazardous waste when discarded. The highly generated ones are epinephrine, m-cresol, phenol, silver sulfadiazine, and multi mineral preparations containing Cr and Se.
4. Hazardous pharmaceutical waste was found to be managed as infectious waste in the hospital under study. Consequently, a management plan was recommended.

Recommendations:

1. Drain or landfill disposal off any waste pharmaceuticals should be avoided, with special emphasis on those that are hazardous.
2. Hospitals have to implement a pharmaceutical waste management program with the aid of Environmental Sector in the Ministry of Health and Population.
3. All hazardous pharmaceutical waste should be treated most commonly by hazardous waste incineration. Thermal destruction of all discarded drugs would provide the highest level of best management practice available at this time. Future technologies, such as plasma arc units, may eventually provide a more environmentally sound option. The ash resulting has to be tested and eventually disposed off in a lined hazardous waste landfill.

The authors would like to thank Mrs. Iman Ahmed El-Sayed, in the Hospital Infection Control Center, for her cooperation during the data collection phase.

Table 1: List of hazardous pharmaceutical waste:

Name of the drug	Indication and use[14]	Reason for being considered hazardous
Arsenic trioxide	Induction of remission in patients with acute leukemia	P-listed
Phentermine	Centrally acting anti-obesity product	P-listed
Epinephrine (adrenaline)	Treatment of acute hypersensitivity, asthmatic attacks, cardiac arrest, and attacks of atrioventricular heart block	P-listed
Physostigmine	Reversing the effect of anticholinergic drugs on CNS	P-listed
Nicotine	Aid in smoking sensation	P-listed
Nitroglycerin	Prevention of angina pectoris	P-listed
Warfarin›0.3%	Anti-coagulant	P-listed
Chloralhydrate	Sedative	U-listed
Paraldehyde	Sedative	U-listed
Chlorambucil	Chemotherapeutic agent	U-listed
Phenol	Disinfectant	U-listed
Cyclophosphamide	Chemotherapeutic agent	U-listed
Reserpine	Antihypertensive	U-listed
Saccharin	Sweetening agent	U-listed
Diethyl stilbesterol	Estrogenic agent	U-listed
Selenium sulfide	Antiseborrheic, antifungal	U-listed
Hexachlorophene	Used as surgical scrub and bacteriostatic for skin cleansing	U-listed
Streptozotocin	Chemotherapeutic agent	U-listed
Lindane	Treatment of scabies	U-listed
Melphalan	Chemotherapeutic agent	U-listed
Uracil Mustard	Chemotherapeutic agent	U-listed
Mercury	Thimerosal in Influenza vaccine	U-listed
Warfarin ‹ 0.3%	Anticoagulant	U-listed
Mitomycin	Chemotherapeutic agent	U-listed
Daunomycin	Chemotherapeutic agent	U-listed
Resorcinol	Treatment of psoriasis and eczema	U-listed
Erythromycin gel 2%	Topical antibiotic	Ignitable
Flexible collodion	Wart remover	Ignitable
Amyl nitrite inhaler	Used for rapid relief of angina pain	Ignitable
Silver nitrate	Applications used for cauterizing	Ignitable
Thimerosal	Preservative in vaccines	Toxic
m-Cresol	Preservative in human insulin	Toxic
Silver sulfadiazine	Antimicrobial cream for burns	Toxic
Cd, Cr, or Se	Found in multi-vitamin and multi-mineral formulations	Toxic

Table 2: Source of hazardous pharmaceutical waste within Alexandria University Main Hospital (2008):

Department / Drug	Epinephrine	Chlorambucil	Phenol	Cyclophosphamide	Melphalan	Warfarin	Daunomycin	m-Cresol	Silver sulfadiazine	Multi-mineral formulations
Internal Medicine Wards(2)	■		■		■					
Injuries Ward	■		■					■	■	■
Gangrene ward	■		■					■	■	■
Emergencies ward	■		■					■	■	■
Haemorrhage Ward	■	■	■					■	■	■
Leukemia Ward	■			■		■				
Ophthalmology ward	■							■		
Oncology Ward				■			■			
Reception	■	■	■					■	■	■
Pharmacy (4)										
Clinical Pharmacy				■						
Intensive Care Units (3)	■		■					■	■	■
Post -operative Care (3)	■		■					■	■	■
Operating Theatre (3)	■		■					■	■	■
Respiratory Unit	■									
BMT *				■	■			■		
Renal Dialysis Unit										
Poisons Unit	■		■			■		■	■	■
Burns Unit	■								■	
Cardiac Unit	■							■		

* Bone Marrow Transplantation

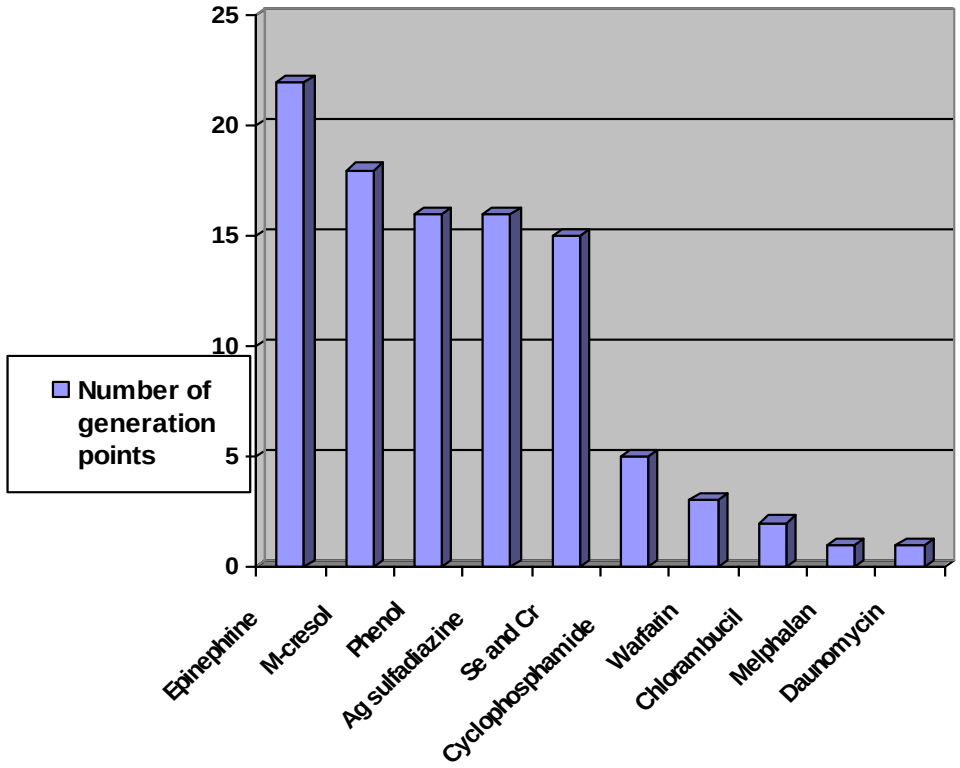

Figure (1): Generation of hazardous pharmaceutical waste from some surveyed points in Alexandria University Main Hospital (2008):

Figure (2): Hazardous pharmaceutical waste inside infectious waste bags and containers.

Figure (3): Door of the storage area for infectious waste and sharps.

Figure (4): Transport vehicle for infectious waste and sharps.

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