(2–4 mg/kg IV, may be repeated after 30 minutes) [1-2, 11].

Other indications for specific antidotes are the poisoning with acetaminophen, anticholinergics, benzodiazepines and certain metal ions. In case of an accidental or suicidal acetaminophen intoxication, acetylcysteine is used. The application should start within 10 hours after the overdose, with 150 mg/kg IV for 15 minutes followed by 50 mg/kg over four hours and 100 mg/kg over 16 hours [12].

If life-threatening effects of anticholinergics like arrhythmias occur, they should be antagonised by physostigmine (which is also toxic in itself). The single dose is 0.04 mg/kg IV or IM (children: 0.5 mg) and should be repeated until symptoms disappear [13].

Flumazenil [single dose 0.2 mg (children over one year old: 0.01 mg/kg IV) over 15 seconds] reverses the sedative effect of benzodiazepines, but because it has a shorter duration of action repeated doses may be needed [14].

Penicillamin is used to chelate metals like lead, mercury or copper. Treatment starts with 300 mg four times daily (children up to 100 mg/kg and a maximum daily dose of 1,050 mg) and should not exceed 40 mg/kg daily if it is continued over a couple of weeks [15].

Conclusion

Although many antidotes currently in use have toxic properties they are indispensable in severe cases of poisoning. Unfortunately, there is no generally accepted European guideline for the treatment of intoxications due to the differing availability of certain antidotes.

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Medication Safety Forum

Totally automated and integrated oncology pharmacy: a matter of fact

Ilaria Uomo, PharmD

Ancona University Hospital has helped develop an advanced chemotherapy preparation system. This has improved the system for providing individual doses.

The preparation of chemotherapy is a complex process that involves many stages and specialists. Due to the high toxicity and low therapeutic ratio of the cytotoxic drugs, a small alteration in the dosage could cause severe harm to the patient and compromise the therapeutic efficacy. Cytotoxics have to be handled safely and efficiently to prevent operators from becoming contaminated and patients from being given the wrong drug.

Potential sources of errors can be categorised by the following stages: prescription; transcription; preparation; delivery; administration. The recent evidence of increasing numbers of medication errors has drawn considerable attention to the risk associated with adverse drug events and the requirement for patient and operator safety.

Information technology has been shown to reduce medication errors at every stage in drug prescription and administration. The automation of hazardous manual activities, together with the introduction of additional checking represents a crucial step towards cutting down clinical risk and making the whole workflow traceable.

With this in mind, the Pharmacy of the University Hospital of Ancona, Italy, has been involved with introducing and validating an oncology robot that brings automation and information technology into day-to-day clinical activities.

The APOTECAchemo system

APOTECAchemo is an automatic system with a robotised arm that prepares antitumour drugs, developed from early versions of the Cytocare system. The system prepares injectable solutions into a microbiologically controlled environment, minimising human exposure to toxic agents and the risk of injury (pharmacy staff safety). Furthermore, at each step the system checks thoroughly using barcode scanners, computerised visual controls and high-precision weight checks (patient safety).

In April 2007, the robot was installed in the pharmacy and exhaustively validated to assess the overall safety of the system, which included the machine's performance, dose accuracy and precision, microbiological and chemical contamination of air, surfaces and disposables, airflow qualification and cleaning efficiency. Then, the technology was gradually introduced into the daily pharmacy routine in order to evaluate its performance in daily operation.

Table 1: Drugs handled by APOTECAchemo

alemtuzumab	liposomal cytarabine*	interferon alpha*	panitumumab
bendamustine*	dacarbazine	infliximab*	pemetrexed
bevacizumab	daunorubicin	irinotecan	rituximab
bleomycin	docetaxel	calcium levofolinate	temsirolimus*
bortezomib	doxorubicin	melphalan*	tocilizumab*
busulfan	liposomal doxorubicin	methotrexate	topotecan*
carboplatin	epirubicin	mitomycin	trabectedin
cetuximab	etoposide	mitoxantrone	trastuzumab
cisplatin	fludarabine	ondansetron*	vinblastine
cladribine	fluorouracil	oxaliplatin	vincristine
clofarabine*	gemcitabine	paclitaxel	vinorelbine
cyclophosphamide	idarubicin	palonosetron*	zoledronic acid
cytarabine	ifosfamide*	pamidronic acid	

*Drugs in validation.

During 2008, we focused on validating the use of a variety of disposables for infusion, such as bags, syringes and elastomeric pumps, as well as on increasing the number of drugs and vials handled by the system. The robot's settings can be adjusted for dimension, viscosity, volume and handling instructions for different drugs; 2009 was devoted to revising the pharmacy workflow in order to improve productivity and use resources more efficiently. The best ways of working were identified and implemented. At the same time, the performance analysis led to the release of a new generation robot with higher productivity and better ergonomics, which was installed in November 2009.

Integration into pharmacy work

Finally, in 2010 we focused on setting up an oncology workflow system that met our quality and safety requirements. APOTECAchemo was integrated into an oncology information system that follows the patient throughout his cancer therapy: e-admission; e-consultation; e-prescription; automated preparation; verification of all aspects of the prepared dose, e.g. independent verification of the prescribed and dispensed doses; e-delivery; e-administration; e-discharge.

Nowadays, over 90% of routine pharmacy work is automated. Between 1,300 and 1,500 preparations are prepared monthly with APOTECAchemo, using 51 different active ingredients, see Table 1. The preparation time for a fluorouracil bag is currently 155 seconds, against 300 seconds for the first generation robot. Nevertheless, the 100% checking of treatments sent to the ward represents the real added value.

Over 96% of preparations show a dose error lower than 5%, and only 0.2% are non-compliant after an error exceeding 10%, the limit fixed by the *Pharmacopoeia*. This statistical appreciation of the error comes from the difference between the dose obtained with the volumetric dosing device, which uses commercial syringes, and the subsequent gravimetric verification by calibrated precision scale.

Since May 2010, 435 chemotherapeutic protocols have been reviewed and validated, 392 patients treated and 4,182 preparations traced from prescription to administration. Besides providing a completely documented and traceable process, the integrated system has brought to light great opportunities for interdepartmental dialogue for re-engineering the process. Since the beginning, the Haematology Clinic has radically reduced patient waiting time and the Pharmacy is delivering the treatments on schedule.

Conclusion

The system has been successfully integrated into the hospital routine, demonstrating the feasibility and advantages of automated preparation of anticancer drugs. High standards of productivity and a big step forward in the quality of the preparation are the initial objectives that have been achieved.

Ancona University Hospital Pharmacy worked with manufacturer Loccioni to formally validate the APOTECAchemo robot in our hospital during 2009. Thanks to tight collaboration of the pharmacy team with the manufacturer, the robot is now able to prepare a wide variety of treatments routinely and interface with the hospital's electronic systems. APOTECAchemo has since become commercially available and is now being used in several large hospitals. More information is available from: www.humancare.loccioni.com/

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