Hazardous drugs handling in hospital: a standardized toxicological screening method to evaluate occupational risks

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ESCP 3rd European Symposium on Clinical Pharmacy — Implementing Clinical Pharmacy in Community and Hospital Settings: Sharing the Experience — 25 - 27 Oct 2007 — Istanbul, Turkey

BACKGROUND & OBJECTIVES

In hospital setting, employees may be exposed to hazardous drugs. Risks and protective measures needed when handling parenteral cytotoxic drugs are well described, whereas information related to drugs like monoclonal antibodies or antivirals are lacking. We developed a standardized method to evaluate drugs potential toxicity and occupational risks. The pharmaceutical forms of the drugs have been taken into account to balance the risks.

DESIGN

We developed an algorithm *(Fig.1)* for toxicity evaluation using Material Safety Data Sheet and their **R**isk and **S**afety phrases[1] , International Agency for Cancer Research (IARC) classification[2] and official manufacturers' data[3].

1. Evaluation of chronic toxicity: mutagenicity and carcinogenicity (R45, R46, R49 or IARC group 1, 2A or 2B or other official data) *(Table 1 & 2)*, acute toxicity: sensitisation or irritation in contact with skin, with eyes or by inhalation (R20-28, 34-38, 41-43; S22-28, 36-39) *(Table 3)* and toxicity to reproduction (R60-63; cat. D, X or other official data) (*Table 4)*
2. Ponderation of toxicity according to the pharmaceutical forms *(Table 5)*
3. Assessment of protective measures (centralization of drug preparation in the pharmacy, wearing of mask, gloves and/or glasses) *(Table 6)*

Table 1 & 2: Determination of protective measures related to chronic toxicity

	MUTAGENIC		
CARCINOGENIC	YES	?	NO
YES	3	2	2
?	2	2	2
NO	2	2	1

Classes of chronical toxicity	Risk of contact by inhalation due to pharmaceutical form		Risk of skin contact due to pharmaceutical form	
	YES	NO	YES	NO
3	(preparation) (administration)	Ø	(preparation) (administration)	Ø
2		Ø		Ø
1	Ø	Ø	Ø	Ø

Table 3: Determination of protective measures related to acute toxicity

Irritating to respiratory system	Risk of contact by inhalation due to pharmaceutical form	
	YES	NO
YES		Ø
?	Ø	Ø
NO	Ø	Ø

Irritating to skin	Risk of skin contact due to pharmaceutical form	
	YES	NO
YES		Ø
?	Ø	Ø
NO	Ø	Ø

Irritating to eyes	Risk of eyes contact due to pharmaceutical form	
	YES	NO
YES		Ø
?	Ø	Ø
NO	Ø	Ø

Table 4: Determination of protective measures related to toxicity to reproduction

Toxic to reproduction	Risk of contact by inhalation due to pharmaceutical form		Risk of skin contact due to pharmaceutical form	
	YES	NO	YES	NO
YES	/	Ø	/	Ø
?	/	Ø	/	Ø
NO	Ø	Ø	Ø	Ø

/ = Pregnant women should NOT handle the product / those who want to be pregnant should wear a mask to handle the product
/ = Pregnant women should NOT handle the product /those who want to be pregnant should wear gloves to handle the product

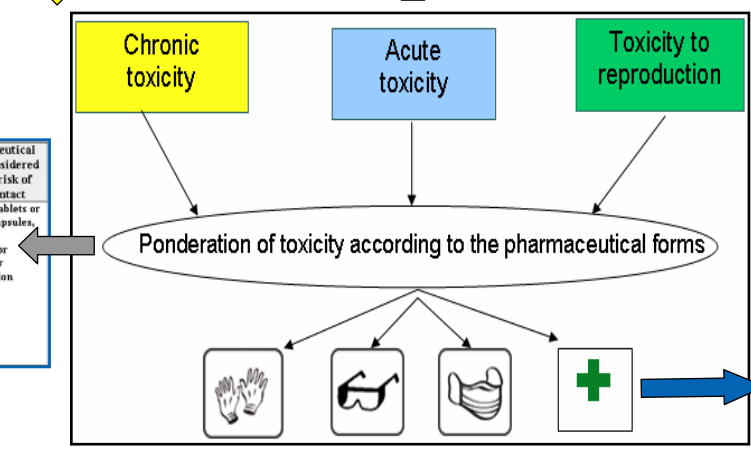

Table 5: Risk of contact related to the pharmaceutical forms

Pharmaceutical forms considered to be at risk of inhalation	Pharmaceutical forms considered to be at risk of skin contact	Pharmaceutical forms considered to be at risk of eyes contact
- crushed tablets or opened capsules, - powders (for iv or oral administration), - sprays, - powders or liquids for nebulization	- crushed tablets or opened capsules, - oral liquids, - powders (for iv or oral administration), - iv infusion, - ointments, - sprays, - powders or liquids for nebulization	- crushed tablets or opened capsules, - sprays, - powders or liquids for nebulization

Table 6: Determination of final protective measures

	Chronic toxicity after ponderation Classes 1 & 3	Acute toxicity after ponderation	Results
Wearing gloves	+	+	
	+	-	
	-	+	
	-	-	Ø
Wearing glasses	+	+	
	+	-	
	-	+	
	-	-	Ø
Wearing mask	+	+	
	+	-	
	-	+	
	-	-	Ø
	Chronic toxicity after ponderation Classe 3	Acute toxicity after ponderation	Results
Centralization of drugs preparation in the pharmacy	+		

Fig. 1: Algorithm for toxicity evaluation

RESULTS

Occupational risks of 14 parenteral monoclonal antibodies, 8 oral and 5 parenteral antivirals, 12 oral cytotoxics and 43 other drugs were analysed. According to our algorithm, crushing of 36% of the 33 tablets forms should be done in the pharmacy (eg. valganciclovir). Only 1 parenteral antiviral should be reconstituted at the pharmacy (ganciclovir). Monoclonal antibodies were found not to be at risks of mutagenicity or carcinogenicity and only gloves will be recommended for their manipulation. No "class-effect" has been pointed out (eg. only a few antivirals were found to be hazardous). 31 products were at risks for pregnant women. Protective measures to be taken by pregnant nurses or those wishing to have a baby will be discussed.

Table 7: Example of results for ganciclovir (Cymevene®)

Brand name	INN	Pharmaceutical form	Administration route	Risk of contact by inhalation due to pharmaceutical form	Risk of skin contact due to pharmaceutical form	Mutagenicity	Carcinogenicity	Chronic toxicity classes	Protective measures related to chronic toxicity	Irritating to respiratory system	Irritating to skin	Irritating to eyes	Protective measures related to acute toxicity	Final protective measures	Toxicity to reproduction	Protective measures for pregnant nurses or those who want to be pregnant
Cymevene®	Ganciclovir	Powder for infusion	iv	Yes	Yes	Yes (R46)	Yes (possible)	3	/ (administration)	Yes (S38)	Yes (S36/37)	Yes		/ (administration)	Yes (R60/61)	/

CONCLUSIONS

Toxicity evaluation of hazardous drugs handling in hospital should take the pharmaceutical forms into account as some toxic drugs may not be associated with occupational risks (eg. coated tablets). Our method allows a standardized way to evaluate whether a drug should be treated as hazardous or not. A table summarizing the proposed protection measures for the studied drugs will be published on our website. Results will be discussed institutionally in order to implement applicable policies and procedures.

References: 1) http://info.anu.edu.au/hr/OHS/_Procedure_Attachments/Risk_and_Safety_Phrases.pdf 2) http://monographs.iarc.fr/ENG/Monographs/index.php 3) www.kompendium.ch

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