Monoclonal antibodies' handling: toxicological evaluation and survey of practices in Swiss hospitals

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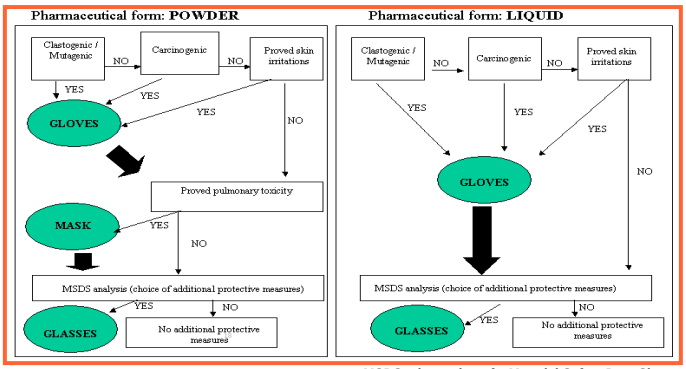
BACKGROUND

Monoclonal antibodies (Mabs) are often used at Geneva University Hospital (HUG). Risks taken by the handler when preparing or administering these new therapeutic agents with complex mechanisms of action are often unknown and clear official information is missing. We performed a study to evaluate how Mabs are manipulated in Swiss hospitals and to determine the toxicity related to Mabs for the handler.

OBJECTIVES

- Survey of practices of Mabs' handling in Swiss hospitals
- Evaluation of nurses' perception of the toxicity related to Mabs' handling in HUG wards
- Toxicological evaluation and risk classification of Mabs



MSDS: shortening of « Material Safety Data Sheet »

Fig. 1: Algorithm used for toxicological evaluation of Mabs

DESIGN

- Standardised questionnaires to 43 Swiss hospitals chief-pharmacists
- Semi-structured interviews of 9 nurses using frequently Mabs in their wards
- Based on literature review and recommended protective measures for the handling, a classification of 15 Mabs in 4 toxicity classes was performed by a pharmacist and a toxicologist (Fig. 1 & 2)

Toxicity class	Proposed protective measures
Class 1:	gloves + glasses + mask
Class 2:	gloves + glasses
Class 3:	gloves
Class 4:	no protective measures

Fig. 2: Toxicological classification of Mabs

RESULTS

Practices in Swiss hospitals:

- Twelve of 43 (28%) of Swiss hospital pharmacies answered the questionnaire
- Preparation of Mabs with oncological indications is centralized at the pharmacy in 5 (42%) hospitals. In only 1 hospital all Mabs are prepared by the pharmacy
- Recommandations for transport or waste management differ among hospitals
- Regular handlers' medical examination is performed in only 25% of the hospitals

Nurses interviews in wards using Mabs: (Tab. 1)

- Four of 9 nurses (44%) considered Mabs as hazardous drugs (cited eg 3x rituximab, 2x trastuzumab, 1x adalimumab, 1x infliximab, 1x palivizumab)
- Only 2 wards prepared Mabs in a dedicated area
- Only 1 ward used rigid containers for hazardous drugs for Mabs' waste management
- Estimation of number of manipulations by nurses was less than 3/week/nurse in 6 (56%) wards and between 3 and 5 in 2 (22%) wards

Toxicological evaluation and protective measures to be recommended at HUG: (Tab. 2)

- Gemtuzumab-ozogamicin was associated with the highest handling risk (class 1), followed by cetuximab, bevacizumab, alemtuzumab and rituximab (class 2) and then infliximab (class 3). For all other Mabs, no protective measures are recommended (class 4)

Tab.1: Sample of nurses interview

	Wards	Drugs regarded as dangerous by nurses	Protection measures in wards		
			Gloves	Glasses	Mask
Wards using not often cytotoxic drugs	A	Rituximab/ Infliximab	Yes	No	No
	B	Rituximab	Yes	No	No
	C	Rituximab / Cetuximab / Gemtuzumab-ozogamicin / Trastuzumab	Yes	No	No
	C	Basiliximab	Yes	Yes	Yes
	E	Alemtuzumab	Yes	No	No
Wards using frequently cytotoxic drugs	F	Rituximab / Trastuzumab	Yes	Yes	Yes
	G	Rituximab / Trastuzumab	Yes	Yes	No
	H	Rituximab / Cetuximab / Infliximab / Alemtuzumab	No	No	No
	I	Alemtuzumab	Yes	No	No

♦ : Wards with special working place for manipulation of cytotoxics and Mabs
♣ : Wards with vertical laminar air flow hood

Tab.2: Mabs toxicological classification

Product and INN	Nb of vials used in the HUG in 2004	Pharmaceutical form	Mutagenic	Carcinogenic	Pre-clinical or clinical studies that proved skin irritation	Pre-clinical or clinical studies that proved pulmonary toxicity	Protection measures recommended for manipulation at HUG: Gloves	Glasses	Protection mask	Class of toxicity
Mylotarg® Gemtuzumab ozogamicin	8	Powder	Yes	Not studied	No	Yes	Yes	Yes	Yes	1
Erbitux® Cetuximab	855	Liquid	No	Not studied	Yes	No	Yes	Yes	No	2
Avastin® Bevacizumab	28	Liquid	Not studied	Not studied	No	No	Yes	Yes	No	2
Mab Campath® Alemtuzumab	96	Liquid	Not studied	Not studied	No	No	Yes	Yes	No	2
Mab Thera® Rituximab	1182	Liquid	Not studied	Not studied	Yes	No	Yes	Yes	No	2
Remicade® Infliximab	838	Powder	No	No	No	No	Yes	No	No	3
Simulect® Basiliximab	113	Powder	No	Not studied	No	No	No	No	No	4
Zenapax® Daclizumab	158	Liquid	No	No	No	No	No	No	No	4
Humira® Adalimumab	28	Liquid	No	Not studied	No	No	No	No	No	4
Raptiva® Efalizumab	0	Powder	Not studied	Not studied	No	No	No	No	No	4
Reopro® Abciximab	1023	Liquid	No	Not studied	No	No	No	No	No	4
Synagis® Palivizumab	23	Powder	Not studied	Not studied	No	No	No	No	No	4
Herceptin® Trastuzumab	206	Powder	No	Not studied	No	No	No	No	No	4
Orthoclone OKT3® Muromonab CD3	3	Liquid	Not studied	Not studied	No	No	No	No	No	4
Tysabri® Natalizumab	0	Liquid	No	No	No	No	No	No	No	4

CONCLUSIONS

This study highlights the lack of standardized practice in the handling of Mabs in Swiss hospitals. Mabs with oncological indications are perceived by nurses at a higher risk than other Mabs, and most of them (exception: trastuzumab) were effectively associated with some degree of potential toxicity in our evaluation. Recommendations for the Mabs' handling should be implemented based on documented toxicological data.

This study is the first part of a major toxicological evaluation of potentially hazardous drugs in order to develop institutional protective guidelines for transport, preparation and administration of these drugs.

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