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Biological monitoring guidance values for chemical incidents

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HIGHLIGHTS

- Biological monitoring is a useful tool to assess chemical exposure.
- Guidance values are available.
- It is important to understand the basis of the guidance values.
- Specific guidance values for incidents would be helpful.

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ABSTRACT

Biological monitoring is a useful tool to assess occupational and environmental exposure following a wide range of chemical incidents. Guidance values are available from international organisations to help interpret the result of biological monitoring. In addition, guidance values based on the 90th percentile of biological monitoring data obtained under conditions of good exposure control may help identify lapses in control and the need for remedial action to improve controls and reduce risk. In all cases interpretation of biomonitoring results following incidents needs care and in particular reference to the time of sample collection and basis of the guidance values. Biomonitoring guidance values specifically derived for chemical incident scenarios are not available but would be of great help to interpret biological monitoring results.

1. Introduction

Biological monitoring is a useful tool for assessing human systemic exposure to hazardous substances by inhalation, ingestion and absorption through the skin. In the workplace it also has a role when control of exposure relies on personal protective equipment. Regular monitoring helps to reassure workers their exposure continues to be well controlled but as this special issue of Toxicology Letters clearly shows, biological monitoring can also help in incidents when control is lost. Such loss of control may range from the comparatively minor incidents within a workplace to major events where people well beyond the workplace may be exposed. Biological monitoring can serve several purposes in the aftermath of a chemical incident. For instance, it can confirm the presence or absence of internal exposure in subjects potentially exposed; it can help relate clinical symptoms to an exposure or can support medical care (Scheepers et al., 2011). The important need to consider the use of biological monitoring in the response phase of an incident was recognised by the World Health Organisation (WHO, 1997, 2009). Depending on the type and scale of the incident it may be necessary to assess the exposure of the workers, first responders or the public. Critical to the utility of biological monitoring is the availability of quality assured analytical methods from accredited laboratories and guidance values to put the results in perspective.

2. Sources of guidance values

There are no biological monitoring guidance values specifically for chemical incident scenarios. The two major sources of biological monitoring guidance values relate to either occupational or environmental exposure. Examples of workplace guidance values are those produced by the American Conference of Governmental Industrial Hygienists (ACGIH, 2013) the German Science foundation (DFG, 2012), the UK Health & Safety Executive (HSE), the French Agency for Food, Environmental and Occupational Health & Safety

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(ANSES, 2013) and the European Scientific Committee on Occupational Exposure limits (SCOEL, 2014). Biological monitoring guidance values for occupational exposure are usually derived from peer-reviewed ethically-approved volunteer and workplace studies that enable a relationship to be derived between a biomarker and an absence of ill-health, airborne occupational exposure limit and/or acceptable level of exposure.

Guidance on environmental exposures comes from studies of biomarkers in the general population like the US national Health and Nutrition Survey (CDC, 2013) and the German Human Biomonitoring Commission (Umwelt Bundesamt, 2014). These are often expressed as 95th percentile reference ranges or, increasingly, based on the "Biomonitoring Equivalents" concept (Hays et al., 2007) where "acceptable exposures" are identified from, for example, tolerable daily intake doses.

3. Limitations

Biological monitoring guidance values for both environmental and occupational exposures are derived for specific purposes and have limitations when applied outside these. One of the major limitations is the relatively small number of them in comparison to the number of substances to which people may be exposed. This is in part due to the costs of population studies and the availability of studies in the peer-reviewed literature linking biomarkers to health or exposure. This is a particularl problem for carcinogens, mutagens and sensitisers where it may be difficult to establish health-based guidance values. In some cases it may be possible to establish guidance values based on the acceptable levels of exposure control. One example of this type of value is the 'benchmark' approach used in the UK based on the 90th percentile of data from workplaces where it has been judged that there is good control of exposure. Although not health-based this type of guidance value is useful for assessing lapses in control and the need for remedial action. Examples include biological monitoring guidance values for sensitisers (isocyanates) and carcinogens (hexavalent chromium, 4,4′methylene bis(2-chloroaniline) methylenedianiline and polyaromatic hydrocarbons) (HSE, 2005). This type of control-based guidance value requires fewer data and can be revised as technology and controls improve (Cocker et al., 2009; Keen et al., 2011). This 90th percentile approach may be suitable for the derivation of in-house guidance values and an aid to improving control by targeting action at the highest exposures.

One of the potential problems of using occupational biological monitoring guidance values after chemical incidents comes from the data used to propose the guidance values which is usually based on a defined exposure period (usually 8 h) and a defined sample collection time related to the half-life of elimination of the substance or its metabolites Substance with short half-lives are usually sampled at the end of exposure or end of shift and samples collected at other times should not be compared to occupational guidance values. Sampling for substances with longer half-lives is less critical but variance caused by diurnal variation may be reduced if sampling is done at the same time each day (Akerstrom et al., 2014). If exposure to long half-life substances is repeated over the work week, there may be a gradual increase in biomarker levels with time. In these cases the guidance values should only apply after several weeks or months of exposure. In addition, occupational biological monitoring guidance values are derived from studies of people of working age who may have different physiological and metabolic responses to the general population. The possibility of saturation of metabolic pathways with high exposures and multiple sources of exposure in incidents should also be considered. In all cases the documents supporting the guidance value should be consulted to establish its basis and relevance for use interpreting results after an incident.

An example of the use of occupational BMGVs was given by Scheepers et al. (2011) who showed by means of a fictitious case of a benzene spill based on a documented chemical incident, how occupational biological monitoring data can be used in a chemical incident scenario. In this case, the aim was to determine the longest time after the incident that urine samples should be collected in order to assure detectable levels of the biomarker. In addition, Scheepers et al. (2011) make reference to several chemical incidents where biological monitoring proved successful; these include incidents with mercury, methyl mercury, PCBs and dioxin. They also mention the successful use of protein adducts as biomarkers in the case of sulphur mustard, acrylamide, ethylene oxide, dichlorvos and acrylonitrile.

Another example of the utility of biological monitoring was reported by Jones and McCallum (2011). This involved a workplace 'incident' in which tunnelling workers were exposed to levels of benzene that exceeded exposure limits. Biological monitoring (urinary S-phenylmercapturic acid levels) revealed high internal exposures to benzene despite the use of personal protection equipment Investigation showed this was due a combination of environmental and human factors. Improvements in protective equipment, work practices and worker behaviour led to significant reductions in exposure.

For first responders to major incidents with no 'normal' exposure to the substance and relying on personal protective equipment for control of exposure the more appropriate guidance values may be those derived from background/population levels. If the equipment is working and being used correctly it might be expected that systemic exposure will be low. However, in these cases and also for those potentially exposed in the wider population, care should be taken interpreting the results. Although population studies are very helpful in assessing the overall exposure of the population they are more difficult to interpret for the individual. Samples are usually collected at times that are not defined in relation to exposure (extent or frequency) and may show considerable intra-individual variation (Aylward et al., 2014).

4. Use of Acute Exposure Reference Values

Since biological monitoring guidance values for both environmental and for occupational exposures have their limitations in the aftermath of a chemical incident, there is a need for biological guidance values specific for use in such incidents. Biological guidance values help assess systemic exposure but are related to external exposure dose metrics. Acute Exposure Reference Values (AERVs) such as AEGLs (EPA, 2012) or Emergency Response Planning guidance Levels (ERPGs AIHA, 2013) are external exposure guidance values specifically derived for chemical incidents (Bos et al., 2013). This guidance can be used in support of the public health management of chemical incidents and should enable comparison of the public health impacts of the chemical exposure and of the possible emergency response measures such as shelter-in-place or evacuation. Such guidance values have at least three tiers (representing action levels) showing the following characteristics:

1. A threshold for discomfort or other minor, rapidly reversible health effects.
2. A threshold for disabling (escape impairing) or otherwise serious health effects; these are not necessarily readily reversible.
3. A threshold for life-threatening effects or lethality.

The eldest programs for derivation of AERVs are the Emergency Response Planning Guidelines (ERPGs) and the Acute Exposure Guideline Levels (AEGLs), both initiated in the US. Following these initiatives, some European Member States have developed comparable methodologies for the derivation of AERVs (for an overview and comparison, see Bos et al., 2013). Within the present context, the AEGL program provides the most suitable and most extensive information and AEGLs are the most used worldwide. The second tier (i.e. AEGL-2) can be regarded as the most important from a health risk point of view and can be considered as the most appropriate external guidance value to serve as basis for a biological guidance value. At present, no methodology to derive these values is available. A concept for the derivation of Biomonitoring Equivalents (BE) to interpret biomonitoring information has been proposed (Hays et al., 2008; Hays and Aylward, 2009). This concept describes how information on kinetics can be used to estimate the concentration of a chemical (or its metabolite) in a biological medium that is equivalent with an existing external guidance value. Although this concept is developed for chronic exposures, it may be worthwhile to verify its applicability to AEGLs which are derived for single exposures. However, it should then be realised that significant differences exist in the derivation and applicability of guidance values for chronic exposure and AERVs, and these should be taken into account. For some chemicals, AEGL values have been derived by physiologically based pharmacokinetic (PBPK) models (Bruckner et al., 2004; Boyes et al., 2005; Bos et al., 2006). These models can directly be used to derive BEs for these chemicals. It has been recommended to derive specific guidance values for professional first responders, in addition to AERVs (Bos et al., 2013).

In the UK, Public Health England (then the Health Protection Agency) set up a working group to review the most common substances identified in public health chemical incidents and to determine whether human biomonitoring could be useful in such instances (HPA, 2011). Some of the most frequently identified substances (ammonia, chlorine, inorganic acids) were unsuitable for biomonitoring assessments whereas others (carbon monoxide, organophosphorous pesticides) could have biomonitoring results directly interpreted against early health effect guidelines. A further set of around 17 chemicals (of the top 30 reported agents) were suitable for human biomonitoring. The group produced protocols for each suitable chemical and collated the available interpretation (usually background reference ranges and occupational guidance values). Recognising the difficulties of arranging appropriate sample collection within a reasonable timeframe of an incident, sampling kits were prepared and made available in Accident and Emergency departments. Maintaining the currency of such kits and knowledge of their existence and use for infrequent occurrences, such as chemical incidents, is an on-going challenge.

5. Conclusions

Biological monitoring is a useful aid to the assessment of systemic exposure following chemical incidents. Biological monitoring guidance values are available for many substances following occupational and environmental exposure and these may help give a perspective on the biomonitoring results from incidents although the documentation supporting the guidance values should be consulted to establish their application and relevance. Biological monitoring guidance values specifically derived for chemical incidents are preferable but are currently lacking. These guidance values may, in future be derived from Acute Exposure Reference Values.

Conflict of interest

The authors declare that there are no conflicts of interest.

Transparency document

The Transparency document associated with this article can be found in the online version.

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