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Characterising glyphosate exposures among amenity horticulturists using multiple spot urine samples

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ABSTRACT

Background: Glyphosate has recently received much public attention following its 'Group 2A – probably carcinogenic to humans' classification from the International Agency for Research on Cancer. Despite the widespread use of glyphosate, there is limited data on potential exposures during common occupational uses.
Objective: The study aimed to characterise occupational exposures to glyphosate among amenity horticulturists through the collection and analysis of urine samples following pesticide application. The impact of work practices on personal exposure, as well as suitability of collecting multiple spot urine samples as a sampling strategy for the assessment of occupational exposure for glyphosate were also examined.
Methods: A minimum of three spot urine samples were collected per work task; before the work task began, after the work task completion and the following first morning void. All samples were analysed separately for glyphosate using liquid chromatography tandem mass spectrometry and for creatinine. Differences in urinary glyphosate concentrations between the pre-task samples versus the post-task and the peak urinary samples were both analysed using paired Student t-tests. Determinants of exposure on glyphosate urine concentrations were evaluated using Pearson's correlation coefficients and linear regression. A multivariate mixed effect model were elaborated to compare the glyphosate concentrations between post-task and following first morning void samples. In these models, worker identity was entered as a random effect to account for the presence of correlations between repeated measurements from the same individuals.
Results: Peak urine glyphosate concentrations measured for work tasks were 2.5, 1.9, 1.9 and 7.4 $\mu g\,L^{-1}$ (arithmetic mean, geometric mean, median and maximum value, respectively). Concentrations were highest in samples taken up to 3 h after completing the work task. Regression analysis showed that workers who sprayed the day before the sampling task had higher glyphosate concentrations in pre-task samples than those who did not spray the day before ($p < 0.01$). Similarly, workers who took breaks during the work task had higher peak urinary glyphosate concentrations ($p < 0.01$). The multivariate mixed effect model showed that the following first morning void samples were approximately a factor 0.7 lower than post-task values.
Conclusion: Occupational exposures to glyphosate among amenity horticulturalists are greater than those reported in environmental studies and comparable with previously reported agricultural studies. A suitable sampling strategy for occupational exposures to glyphosate is the collection of a spot urine sample up to 3 h after completing the application of a glyphosate based pesticide product, which provides a reliable marker of peak exposure.

1. Introduction

Glyphosate, a broad spectrum post emerging herbicide, has recently received international attention due to its 'Group 2A – probably carcinogenic to humans' classification by the International Agency for Research on Cancer (IARC, 2016). The IARC classification differs to that of the European Chemicals Agency (ECHA, 2017), the European Food Safety Authority (EFSA, 2017), the United States Environmental Protection Agency (US EPA, 2016a) and the Food and Agriculture Organization of the United Nations of the World Health Organization

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(JMPR, 2016). EFSA have established an Acceptable Daily Intake (ADI) value of 0.5 mg/kilogram of body weight per day (mg/kg bw/day) and an Acceptable Operator Exposure Level (AOEL) of 0.1 mg/kg bw/day for glyphosate (EFSA, 2015). Despite the widespread use of glyphosate, few publically available studies have investigated potential exposures during common occupational uses. There is also an increasing concern with respect to chronic low dose exposure of glyphosate based pesticides and adverse renal (Myers et al., 2016) and hepatic (Mesnage et al., 2017) health effects, with a necessity for studies to investigate this relationship further (Mills et al., 2017).

Biomonitoring is considered a reliable exposure assessment tool for pesticides once pharmacokinetics data is available. Biomonitoring involves the measurement of the pesticide or relevant biomarkers in biological samples such as blood or urine (Acquavella et al., 2003; Chester, 2010; Sexton et al., 2004).

Recently glyphosate has been added to national biomonitoring programmes in Canada (Haines et al., 2017), Germany (Conrad et al., 2017) and the United States of America (USA) (NHANES, 2018). It is generally accepted that more exposure data is required to characterise the range of exposures and to better distinguish exposure variations between individuals and different regions (Hoppe, 2013).

Biomonitoring data for glyphosate has been published for occupational exposures in the agriculture and horticulture sectors (Acquavella et al., 2004; Connolly et al., 2017; Curwin et al., 2007; Johnson et al., 2005; Mesnage et al., 2012). In addition, data on environmental exposures in Germany (Conrad et al., 2017; Hoppe, 2013; Krüger et al., 2014; Markard, 2014), the USA (Mills et al., 2017), Sri Lanka (Jayasumana et al., 2015) and in Ireland (Connolly et al., 2018) has also been obtained. Available data suggests that both occupational and environmental exposures do not exceed EFSA's ADI or the AOEL (Niemann et al., 2015).

It is often difficult to draw comparisons between the earlier published exposure studies for glyphosate due to the use of different analytical methods and/or sampling strategies. There is also some uncertainty regarding the half-life of glyphosate in humans (Faniband et al., 2017; IARC, 2016; Williams et al., 2000), which creates ambiguity regarding the sampling strategy that is most appropriate for occupational exposure assessment. Some occupational biomonitoring studies have analysed pooled urine samples collected over a 24 hour (h) period, providing an estimate of average exposure over this sampling period (Acquavella et al., 2004; Lavy et al., 1992; Mesnage et al., 2012). However, this sampling strategy does not allow identification of peak exposures. Others have analysed a spot urine sample as a marker of the 24 h exposure which could result in an under- or over-estimation of the actual exposure concentration (Connolly et al., 2017; Curwin et al., 2007; Scher et al., 2006). A spot sampling strategy may be considered more reliable for environmental exposure studies of the population, where recent occupational or personal use exposure is unlikely (Hinwood et al., 2002). For occupational exposure or regulatory risk assessments, where an estimate of the magnitude of exposure is required: collection and analysis of 24 h urine samples, or multiple spot samples collected over a 24–48 h period should provide a more reliable measure of the true exposure and variability (Kissel et al., 2005). However, this is not always practical or feasible and therefore spot sampling strategies are also needed.

To the authors' knowledge there are just two published studies reporting occupational exposure to glyphosate among amenity horticultural workers. The first study involved the collection of dermal and inhalation samples (Johnson et al., 2005) and the second (published by the authors of the current study) was a biomonitoring study (Connolly et al., 2017). Amenity horticulturists in the UK applied approximately 350,000 kg of glyphosate in a year (2012) (FERA, 2017), whereas the Irish amenity horticulture sector has a production value of over €70 million and employs over 1300 workers (Horticulture Industry Forum, 2017). Connolly et al. (2017) assessed glyphosate exposures by collecting spot urine samples pre- and post-work tasks. Glyphosate exposure concentrations (geometric mean (GM) ((geometric standard deviation) (GSD)) 0.7 (1.1) μg L^{-1}) were detected. Considering the sampling strategy employed and the levels of detectable glyphosate concentrations found in the spot urine samples, the importance of this sector, its reliance on glyphosate and the numbers of horticultural workers that could potentially be exposed to glyphosate, the collection of more exposure data is warranted.

This current study describes the follow-up study, which aimed to characterise exposures within the same occupational group. The study provides a comprehensive assessment of occupational exposures among amenity horticultural workers and examines the impact of work practices on exposure levels. The collection and analysing of multiple spot urine samples collected before, throughout the day and after pesticide applications allowed for an assessment of the suitability of the sampling strategy for occupational exposure assessment.

2. Materials and methods

2.1. Site description and study population

The measurement campaign took place during September 2016 to September 2017. Details regarding the study sites, which were managed by the Irish Commissioners for Office of Public Works (OPW) and the worker recruitment strategy have previously been published (Connolly et al., 2017). Briefly, three similar exposure groups (SEGs) were defined using information about the spraying methods used to apply glyphosate based pesticide products (Table 1; Fig. 1). Recruitment was completed in coordination with the OPW Health and Safety Unit. The lead

Table 1
Characteristics of established similar exposure group (SEG).

Similar Exposure Group	Glyphosate products used (& glyphosate concentration of product)		Description of pesticide spray applicator
	Product	Conc. (g L^{-1})	
Manual knapsack	Roundup Biactive XL Clinic Ace Roundup Biactive Pistol Roundup XL	360 360 360 250 360	A handheld lance connected to a knapsack, carried on the workers back. In this study, workers typically sprayed 10–15 L of the pesticide solution, (approximately 1 part concentrate to 10 parts water). The applicator was used for spot spraying weeds, spraying footpaths and chemical edging around gardens (Fig. 1a).
Pressurised hand held lance	Roundup Biactive XL Pistol Glyfos Rambo 360 Roundup Gold 450	360 250 360 360 450	A handheld lance (100–200 kPa) connected to a motorised portable applicator. Workers typically used 1 part concentrate to 10 parts water for total weed control in large open areas and courtyards (Fig. 1b). One worker used a portable 5 L SteelMaster V5 professional sprayer, a manual handheld lance (operated at 600 kPa), used to spray above head height to maintain the integrity of historic buildings.
Controlled droplet applicator	Nomix Dual Roundup XL	120 360	The controlled droplet applicator has a function where the user can control the droplet size, which reduces spray drift. This applicator is used with a premixed solution, for clearing footpaths and for total weed control (Fig. 1c). Workers used on average, 1–3 L of the pesticide product.