Science of the Total Environment 456–457 (2013) 34–41

Contents lists available at SciVerse ScienceDirect

Science of the Total Environment

journal homepage: www.elsevier.com/locate/scitotenv

Detection of herbicides in the urine of pet dogs following home lawn chemical application

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HIGHLIGHTS

- Lawn chemicals were commonly detected on treated and "untreated" lawns.
- The detection of lawn chemicals in the urine of pet dogs was widespread.
- Lawn chemicals persisted on the grass for at least 48h after application.
- Chemicals persisted longer on grass under certain environmental conditions.
- Dogs may serve as sentinels for human expsoures, and further study is justified.

ARTICLE INFO

Article history:
Received 19 October 2012
Received in revised form 5 March 2013
Accepted 5 March 2013
Available online 10 April 2013

Keywords:
Bladder cancer
Herbicides
Dog
2,4-D
MCPP
Dithiopyr

ABSTRACT

Exposure to herbicide-treated lawns has been associated with significantly higher bladder cancer risk in dogs. This work was performed to further characterize lawn chemical exposures in dogs, and to determine environmental factors associated with chemical residence time on grass. In addition to concern for canine health, a strong justification for the work was that dogs may serve as sentinels for potentially harmful environmental exposures in humans. Experimentally, herbicides [2,4-dichlorophenoxyacetic acid (2,4-D), 4-chloro-2-methylphenoxypropionic acid (MCPP), dicamba] were applied to grass plots under different conditions (e.g., green, dry brown, wet, and recently mowed grass). Chemicals in dislodgeable residues were measured by LC-MS at 0.17, 1, 24, 48, 72 h post treatment. In a separate study, 2,4-D, MCPP, and dithiopyr concentrations were measured in the urine of dogs and in dislodgeable grass residues in households that applied or did not apply chemicals in the preceding 48 h. Chemicals were measured at 0, 24, and 48 h post application in treated households and at time 0 in untreated control households. Residence times of 2,4-D, MCPP, and dicamba were significantly prolonged ($P < 0.05$) on dry brown grass compared to green grass. Chemicals were detected in the urine of dogs in 14 of 25 households before lawn treatment, in 19 of 25 households after lawn treatment, and in 4 of 8 untreated households. Chemicals were commonly detected in grass residues from treated lawns, and from untreated lawns suggesting chemical drift from nearby treated areas. Thus dogs could be exposed to chemicals through contact with their own lawn (treated or contaminated through drift) or through contact with other grassy areas if they travel. The length of time to restrict a dog's access to treated lawns following treatment remains to be defined. Further study is indicated to assess the risks of herbicide exposure in humans and dogs.

Abbreviations: 2,4-D, 2,4-dichlorophenoxyacetic acid; creat, creatinine; dithiopyr, 2-(difluoromethyl)-4-(2-methylpropyl)-6-(trifluoromethyl)pyridine-3,5-dicarbothioate; MCPP, 4-chloro-2-methylphenoxypropionic acid; UC, urothelial carcinoma.

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http://dx.doi.org/10.1016/j.scitotenv.2013.03.019

1. Introduction

Urinary bladder cancer (urothelial carcinoma, UC) causes >14,000 deaths yearly in the United States (Tanaka and Sonpavde, 2011). Approximately half of UC cases are thought to be due to exposure to cigarette smoke and chemicals in the workplace (Dietrich and Golka, 2012; Droller, 2006; Felknor and Delclos, 2006). Exposure to herbicides, pesticides, and contaminants in agricultural chemical mixtures could increase UC risk, although not all studies support this role (Alavanja and Bonner, 2012; Boers et al., 2010; Koutros et al., 2009; Singh et al., 2010). Genetic factors have been associated with increased UC risk, especially in relation to chemical exposures (Franekova et al., 2008; Murta-Nascimento et al., 2007). More than half of UC patients, however, have no known risk factors for the cancer. Studies are needed to further identify environmental and genetic factors, and gene–environment interactions that increase UC risk.

Dogs offer a highly relevant naturally-occurring animal model to identify environmental chemical exposures and gene–environment interactions that increase UC risk. Naturally-occurring UC in dogs closely mimics human invasive UC in physiologic age of onset, molecular features, biologic behavior, and treatment response (Knapp, 2006, 2007). Dogs offer the opportunity to study heritable risk factors and chemical–gene interactions leading to UC as specific breeds of dogs are much more likely to develop this cancer. This breed-associated, i.e. heritable, risk for UC includes an 18–20-fold increased risk in Scottish Terriers and a 3–5-fold increased risk in the genetically-related West Highland White Terriers, and a 3–5-fold increased risk in Shetland Sheepdogs and beagles (Knapp, 2006). With the tremendous genetic diversity in humans, groups of humans with this level of heritable risk for UC have not been identified. In addition, since dogs do not smoke, they can be a more specific sentinel for other causes of UC in humans.

Another intriguing aspect of UC in dogs is the latency period between chemical exposure and UC development. In dogs this can be as short as a year (range 1–10 yr) (Okajima et al., 1981), whereas latency periods in humans can extend to several decades (Dietrich and Golka, 2012; Droller, 2006; Felknor and Delclos, 2006). This indicates that dogs could serve as sentinels to environmental exposures that could be harmful to humans, as well as dogs, if not addressed in a timely fashion. Dogs have already been identified as sentinels for environmental exposures related to the risk of other types of cancer (Reif, 2011), with a notable example being the risk of mesothelioma from exposure to asbestos (Glickman et al., 1983; Kelsey et al., 1998). In a case control study, owners of dogs with mesothelioma were more likely than owners of control dogs to have been exposed to asbestos at work or through a hobby (Glickman et al., 1983). It is considered appropriate to follow the diagnosis of mesothelioma in a dog with a careful search for asbestos in the environment in order to prevent new or continued exposure to humans in the same area.

A significant association between chemical exposure and UC risk has been described in dogs across many breeds (Glickman et al., 1989). A stronger association between lawn chemical exposure and UC risk has been reported in a genetically susceptible dog breed, Scottish Terriers (Glickman et al., 2004). In a case control study, Scottish Terriers exposed to lawn herbicides had a 3.6-fold increased risk for UC (OR 3.62, 95% CI 1.17–11.19, P = 0.03) compared to unexposed dogs. Dogs exposed to lawn herbicides and pesticides had a 7.2-fold increased UC risk (OR 7.19, 95% CI, P = 0.001) (Glickman et al., 2004). It was suggested that chemical carcinogens (or pre-carcinogens) on the lawn were internalized by the dogs and excreted in urine, thereby exposing the urothelium to harmful chemicals.

Herbicides can readily be measured in urine of dogs following experimental administration (Dickow et al., 2001). Similarly, in a community study, 2,4-D was detected in urine of dogs exposed to household lawns treated with herbicides within the previous 42 days (Reynolds et al., 1994). Among 44 dogs potentially exposed to 2,4-D treated lawns, 2,4-D concentrations of at least 10 μg/L were found in 75% of dogs, and concentrations ≥ 50 μg/L were found in 39% of dogs on average 11 days post lawn treatment (Reynolds et al., 1994). The study reported here was performed to confirm and extend these findings in a contemporary setting. The relationship between the herbicide concentration on the grass and the likelihood of exposure of dogs to lawns has not been previously reported. The primary goal of the current study was to prospectively measure herbicide concentrations on treated lawns and in the urine of dogs living in these homes, before and after lawn application, with comparison to concentrations on lawns and in urine of dogs from untreated households. A secondary goal was to identify host and environmental factors that could increase exposure potential.

For the household study, the concentrations of 3 chemicals commonly used in commercial lawn care products were measured including 2,4-dichlorophenoxyacetic acid (2,4-D), 4-chloro-2methylphenoxypropionic acid (MCPP), and dimethyl 2-(difluoromethyl)-4-(2-methylpropyl)-6-(trifluoromethyl) pyridine-3,5-dicarbothioate (dithiopyr). The chemical, 2,4-D, was selected for study because it is commonly included in lawn treatment mixtures and because it has been incriminated as a potential carcinogen in other studies. An association between 2,4-D exposure and risk of cancer, especially non-Hodgkins lymphoma, in humans has been described (Hardell et al., 1981; Hoar et al., 1986; Hoar-Zahm et al., 1990; Landgren et al., 2009; Miligi et al., 2006; Mills et al., 2005; Wigle et al., 1990). A positive association has also been reported between the risk of non-Hodgkins lymphoma in dogs and exposure to lawn chemicals (Takashima-Uebelhoer et al., 2012), and specifically 2,4-D on lawns (Hayes et al., 1991). Not all studies, however, support a link between this chemical exposure and lymphoma in dogs (Carlo et al., 1992; Kaneene and Miller, 1999) or humans (Bond and Rossbacher, 1993; Burns et al., 2011; Garabrant and Philbert, 2002; Hartge et al., 2005). Considerable concern has also been expressed regarding the risk of non-Hodgkins lymphoma and other diseases in Vietnam veterans exposed to a herbicide mixture containing 2,4-D (Agent Orange), although contaminating dioxins could be the most harmful component of this mixture (Hites, 2011). The other 2 chemicals measured in the household study (MCPP, dithiopyr) have not been studied as rigorously as 2,4-D. These chemicals were included in the study because they are commonly used in lawn treatment products, can be accurately measured, and could serve as markers of lawn chemical uptake in dogs.

2. Methods

2.1. Study overview

This study was approved by the Purdue Animal Care and Use Committee and the Purdue Institutional Review Board for human subject use. The two components of the study were: (1) an experimental grass plot study to confirm analytic methods used to measure chemicals on the grass and their residence time under different environmental conditions, and (2) a household study to determine concentrations of lawn chemicals on grass and in the urine of dogs exposed to treated lawns or control (untreated) lawns.

2.2. Experimental grass plot study

2.2.1. Sample grass plots

Sample grass plots were selected from established lawn areas at Purdue University that had been planted with mixed 50% bluegrass/50% fine fescue and which were restricted from any lawn treatment for at least 4 months before beginning the experiments. A 25 meter (m) boundary area surrounding the plots was sequestered from treatments for the same period. The 4 m^2 plots were located in open areas ≥ 8 m from buildings, trees, or shrubs. Two plots were used for each treatment/week. Three samples were collected at each time point from each plot. Within each condition type, assignment of treatment was randomized (random block design). Prior to herbicide