Pesticide-Poisoned Patients: Can They Be Used as Potential Organ Donors?

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Abstract

Introduction The gap between the number of patients on transplant waiting lists and patients receiving transplants is growing. Use of organs from donors who have died following pesticide exposure remains controversial. This study reviews the literature related to transplantation from this group.

Methods A literature search was undertaken on PubMed using the following keywords: ‘insecticide’, ‘pesticide’, ‘rodenticide’, ‘organophosphate’, ‘carbamate’, ‘paraquat’, ‘poisoning’, ‘toxicity’, ‘overdose’, ‘intoxication’, ‘ingestion’, ‘organ donation or procurement’, ‘transplant’, ‘allograft transplant’, and ‘expanded criteria organ donation’; 21 specific pesticides/insecticides were also added to the search; the indexes for EAPCCT/NACCT meeting abstracts 2008–2017 were also searched. Identified publications were reviewed and if described human donation/transplantation of ≥ 1 solid organ(s), the following was extracted: (i) compound(s) ingested; (ii) donor demographics; (iii) organ(s) transplanted; and (iv) graft function at follow-up.

Results Ten papers were identified describing 20 fatalities (1999–2017) related to the following pesticide exposures: organophosphate, 8 cases; aldicarb, 4; paraquat, 3; parathion, 1; malathion, 1; carbofuran/carbamate, 1; carbamate, 1; and brodifacoum, 1 and no further cases were identified from EAPCCT/NACCT abstracts. Donors were aged 12–50 (25.9 ± 11.9) years. Forty-four organs were transplanted: 28 kidneys, 7 livers, 6 corneas, and 3 hearts. Forty recipients had outcome reported: 3 (7.5%) patients died, 3 (7.5%) had graft failure/dysfunction and 34 (85.0%) had good graft function. Overall survival with good function was 96%, 71%, 83%, and 67% for kidneys, livers, corneas and hearts respectively.

Conclusion Review of the published literature suggests that solid organ donation following exposure to a pesticide is associated with good short-to-medium-term graft organ function following transplantation, particularly for transplanted kidneys and corneas.

Keywords Organ transplantation · Pesticides · Insecticides · Poisoning

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Introduction

Each year, more individuals join solid organ donation waiting lists than receive a donation. There are currently 6388 patients in the UK and 114,864 patients in the USA on solid organ donation waiting lists, with 4753 (UK) and 34,771 (USA) patients receiving an organ donation in 2016–2017 [1, 2]. The difference between demand and supply of donor organs is due in part to greater demand from an increasing population life expectancy and improved management of patients with end-stage disease who then become eligible for organ donation. Additionally, there has been a reduction in the number of potential organ donors attributed to a reduction of deaths due to intracerebral events [1–3]. This has increased the demand for organ donors, with the current donor pool unable to grow at the same rate [3]. In an attempt to increase the potential pool

of organ donors, a number of strategies have been used. There is currently a public consultation in the UK to switch from requiring consent for donation from the next of kin or family member, to ‘presumed consent’ where an individual is considered suitable unless they ‘opt’ out or the family directly refuses organ donation [4, 5]. There is also an increasing interest in the use of non-conventional organ donors, including those who die following acute drug or chemical toxicity, such as cocaine, carbon monoxide, and cyanide with reported good graft function following donation from patients who die related to these exposures [6–8].

Clinicians may think that poisoned patients do not make suitable organ donors due to not only the potential risks associated with the toxin(s) involved, but also organ damage due to the toxin themselves. This maybe because toxin/poisoning-related deaths are associated with systemic toxicity and multi-organ involvement. In addition, the perceived risk of potential blood-borne virus(es) in the donor may be greater in some poisoned-related deaths (e.g. use of recreational drugs such as cocaine), and therefore the acceptability of donation of organs may be reduced [6–8]. However, previous surveys of transplant surgeons, clinical/medical toxicologists and intensive care physicians have demonstrate that these groups of physicians consider patients dying from a range of toxins could be potential organ donors [6–8]. These toxins include carbon monoxide, benzodiazepines, barbiturates, tricyclic antidepressants, methanol, cyanide and cocaine [6–8]. In addition, previous studies have demonstrated similar 1-year survival rates to solid organ donation from non-poisoned donors [9, 10]. Patterns of poisoning death differ in developed countries (e.g. Europe, North America and Australasia) where pharmaceutical agents are more commonly involved compared to developing areas (e.g. Asia) where pesticides and similar chemicals remain more commonly involved [11, 12]. In Sri Lanka, where there is a high rate of suicide by pesticide ingestions, clinicians readily harvest organs from those patients for transplantation. As a result, Sri Lanka is a net exporter of donated corneas to other countries, meaning they harvest more than are required for transplant in the country itself [12, 13].

Given the potential systemic toxicity and multi-organ involvement in fatalities involving pesticides and related compounds, there is the potential that clinicians may be less likely to consider using these patients as potential organ donors. In this study, we aim to identify published cases involving pesticide-related death and the outcome following transplantation.

Methods

We undertook a literature search of the PubMed database to identify published articles reporting solid organ (kidney, liver, heart) and/or cornea transplantation from donors

who had died following exposure to a pesticide. Keyword terms used in this search were ‘insecticide’, ‘pesticide’, ‘rodenticide’, ‘organophosphate’, ‘carbamate’, ‘paraquat’, ‘poisoning’, ‘toxicity’, ‘overdose’, ‘intoxication’, ‘ingestion’, ‘organ donation or procurement’, ‘transplant’, ‘allograft transplant’, and ‘expanded criteria organ donation’, along with 21 specific named pesticides ‘malathion’, ‘parathion’, ‘fenitrothion’, ‘deltamethrin’, ‘rotenone’, ‘chlorfenapyr’, ‘diazinon’, ‘fenthion’, ‘dichlorvos’, ‘chlorpyrifos’, ‘ethion’, ‘trichlorfon’, ‘endosulfan’, ‘aldicarb’, ‘carbofuran’, ‘carbaryl’, ‘ethienocarb’, ‘fenobucarb’, ‘oxamyl’, ‘methomyl’, ‘fenoxycarb’ and ‘brodifacoum’ (brand names for these compounds were not used). The search was not limited by year of publication. We chose these pesticides because they were the most commonly encountered pesticides.

In addition, the abstracts from the European Association of Poisons Centres and Clinical Toxicologists (EAPCCT) and North American Congress of Clinical Toxicology (NACCT) congresses from 2008 to 2017 inclusive were also searched using the same terms.

One author reviewed all identified potential articles to determine if they related to human donation and/or transplantation of one or more solid organ(s) and/or corneas following exposure to a pesticide. We extracted the following information from those articles meeting the inclusion criteria: (i) donor demographics (age and gender); (ii) compound(s) exposed to; (iii) what was transplanted; (iv) outcome and/or assessment of graft function at reported follow-up and the duration of this follow-up; and (v) any reported adverse outcome. This information was used to determine organ survival rates of organs from pesticide-related deaths following donation.

Results

Ten articles were identified in the PubMed search describing 20 deaths where organ donation occurred following exposure to a pesticide; no additional reports were identified from the EAPCCT and NACCT abstracts [13–22].

All deaths involved ingestion of the pesticide; there were no deaths related to dermal and/or inhalation exposure. The reported compounds involved (exposures as reported by authors) were aldicarb (4 deaths), parathion (1 death), malathion (1 death), carbofuran/carbamate (1 deaths), organophosphate (8 deaths), carbamate (1 death), brodifacoum (1 death) and paraquat (3 deaths).

The organ donors were aged 12–50 (mean $\pm$ SD age 25.9 ± 11.9) years. Donor organs were retrieved from 10 males and 10 females. There were a total of 44 organs/corneas transplanted (28 kidneys, 7 livers, 6 corneas and 3 hearts) to 40 recipients.

The immediate complications after transplantation, follow-up outcome (range 4–62 months) and graft survival are summarised in Table 1. Of the 40 recipients of donor organs, 36 (90%) had follow-up reported and in these cases, 3 (7.5%) patients had died, 3 (7.5%) had graft failure and/or dysfunction and 34 (85%) were reported to have good graft function. The term ‘good graft function’ was used in the papers we reviewed, but the term was not universally well defined by authors. This equated to an overall survival rate with ‘good graft function’ as 96%, 71%, 83%, and 67% for transplanted kidneys, livers, corneas and hearts respectively (equivalent to a graft failure rates of 4%, 29%, 17%, and 33%).

Discussion

In our study, we identified a number of cases of organ donation with reported good short-to-medium-term graft function where organs were donated from individuals that died following exposure to pesticides. The earliest identified published case was from 1999 and involved successful liver donation from a 21-year-old male who was found unconscious following a seizure with subsequent detection of an intracranial haemorrhage and associated hydrocephalus following a brodifacoum overdose (analytically confirmed

high blood brodifacoum concentrations and deranged coagulation screens). The recipient was a 45-year-old woman with a background of recurrent localised non-metastatic hepatocellular carcinoma secondary to hepatitis B and no metastases: the postoperative clinical course was uneventful, and at 15-month follow-up the donor recipient remained tumor-free with normal liver function [22].

There is an urgent need to increase the organ donor pool to overcome the current deficit between the number of patients on the transplant waiting list and the number of donor organs available. Typically, organ donors that die from poisoning are younger compared to the average age of organ donors and therefore likely to have fewer chronic medical comorbidities [1, 2, 23, 24]. The Organ Procurement and Transplantation Network (OPTN) was established by the US National Organ Transplant Act in 1984 and has been regulated by the US Department of Health and Human Services (HHS) since 2000 [23]. It is a partnership linking those involved in organ donation and transplantation in the USA, which aims to not only increase transplantation rates, but also survival following transplantation. Data from the OPTN shows that over the two decades (1997 to 2017), there has been an increase in the proportion of organ donors aged 50–64 from 20.7 to 27.4% [24]. The average age of the organ donors in this study was

Table 1 Organs transplanted after death following pesticide or insecticide exposure with follow-up outcomes (exposures listed as reported by authors)

Organ	Exposure	Organs transplanted	Follow-up outcome
Kidney	Aldicarb	6	All patients alive with ‘good graft function’ at 7–17 months
	Parathion	2	Patient 1: serum creatinine 1.67 mg/dL (148 µmol/L) at 3 months Patient 2: delayed graft failure due to early humoral rejection requiring haemodialysis at 3 months
	Malathion	2	Both patients reported to be alive with ‘good graft function’ at 12 months
	Carbofuran/carbamate	2	Patient 1: serum creatinine of 1.0 mg/dL (88 µmol/L) and creatinine clearance of 71 mL/min/1.73 mL/min m ² at 12 months (right-transplanted kidney) Patient 2: serum creatinine of 0.9 mg/dL (80 µmol/L) and creatinine clearance of 68.6 mL/min/1.73 mL/min m ² at 12 months (left-transplanted kidney).
	Organophosphate	16	12 patients all and reported to have ‘excellent renal function’ at 13–62 months Data on other 4 patients not reported
Heart	Aldicarb	2	Both patients alive with ‘good graft function’ at 17 and 22 months respectively
	Carbamate	1	Died 24 h post-transplantation due to acute left ventricular dysfunction
Liver	Aldicarb	4	3 patients alive with ‘good graft function’ at 7–17 months 1 patient died post-transplant due to primary non-function
	Parathion	1	Alive at 3 months but had recurrent ascites requiring treatment
	Malathion	1	Alive with ‘good graft function’ at 12 months
	Brodifacoum	1	Alive with ‘good graft function’ (defined by the authors as ‘normal liver function and coagulation studies’) at 15 months
Corneas	Paraquat	6	Two patients reported to have ‘good visual acuity’ at 6 months post-transplantation, but specific visual acuity not reported At 12 months in 3 patients the transplanted corneas maintained transparency. (One additional patient had re-transplantation due to corneal epithelial cell defect

25.9 years old. Younger age, a characteristic of many poisoned patients, may provide an advantage in suitability for organ donation. Typically, prior to death, a poisoned organ donor would receive intensive therapy and organ support on a critical care unit, and thus donor organs are medically optimised when being considered for transplantation. In fatalities associated with acute poisoning, there is often a clear established cause of death with a predictable toxicity. This toxicity can be managed to minimise adverse effects on potential donor organs and/or recipients of the organ(s).

At the American College of Medical Toxicology (ACMT) Annual Scientific Meeting in 2014, the use of interactive clinical case-based discussion workshops around organ donation from deaths after acute poisoning showed that education could significantly increase positive recommendation of organ donation and transplantation demonstrating it is possible to educate healthcare profession about utilisation of this potential organ donor pool of patients [25]. In a previous postal questionnaire conducted in UK transplant centres in 2002 using case scenarios around potential organ donation following deliberate methanol ingestion, cardiac arrest presumed secondary to cocaine overdose, accidental domestic carbon monoxide inhalation and industrial cyanide exposure; over 80% of intensive care directors and up to 100% of transplant physicians/surgeons would consider these organs as potential donors [6].

Graft failure rate in the solid donor organs from this study (kidneys, liver and heart) was compared against the overall graft failure rate at 6–12-month follow-up using data from OPTN [1, 24]. In our current study, there was variable follow-up of recipients ranging from 4 to 62 months. In 2015, overall failure of transplanted (i) kidneys was 4.8% in the OPTN at 6 months compared to 4% when follow-up occurred in this study; (ii) livers was 7.3% compared to 29%; and (iii) hearts was 9.9% compared to 33%. Data for overall corneal donor failure rates was not available. One issue is that the numbers in this study are much smaller compared to the transplantation rates in the OPTN, so the impact of failure of individual transplanted organs will have a more significant impact on overall failure rates. Also, follow-up was only reported at 6 months in OPTN whereas follow-up in our cases was reported at much later, which could have impacted on graft survival. Additionally, the toxin(s) involved in pesticide-related donation may themselves have an impact on graft failure rate, and more widespread utilisation of this potential organ donor population would allow greater understanding of any potential impacts. As noted, duration of follow-up after transplantation varied considerably in the identified articles, although 36 (90%) had ‘short-to-medium-term’ follow-up after organ transplantation to measure outcomes. No recipients were followed up for 5 years or more, so it is not possible to determine the overall long-term graft survival in this organ donor pool.

One limitation of this study is the impact of bias around reporting of these cases, with a greater likelihood of reporting of cases with positive outcome such as survival of recipient and/or good graft function after transplantation. Future studies could look at analysis of organ donor/recipient registries, to try and identify those donations where there is a negative outcome (e.g. graft failure and/or rejection). In addition, it would be useful to look at analysis of referrals to organ donation teams, to determine what proportion of those referred following pesticide deaths are rejected by the organ donor teams outright without proceeding to organ harvesting and/or donation. The extent of the exposure, underlying health of the potential donor, and the treatments following exposure, in addition to the specific pesticide that an individual has been exposed to, will also impact the suitability of an individual to be an organ donor. The choice of the database (PubMed) and abstracts (NACCT/EAPCCT) searched in this study also means not all published cases (in full or in abstract form) may have been identified.

Conclusion

There is an urgent need to identify additional potential donor pools to meet the increasing demand for recipient organs. This review of the published literature suggests that solid organ donation from individuals who die after acute exposure to a pesticide can be associated with good short-to-medium-term graft function. Further work is needed to determine how this potential donor pool can be more widely utilised to address some of the issues around increasing donor waiting lists.

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Compliance with Ethical Standards

Conflict of Interest None

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