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Poisoned patients as potential organ donors: postal survey of transplant centres and intensive care units

David Michael Wood¹, Paul Ivor Dargan² and Alison Linda Jones³

¹Specialist Registrar in General Medicine and Clinical Pharmacology, National Poisons Information Service (London), Guy's and St. Thomas' Hospital, London, UK

²Specialist Registrar in General Medicine and Toxicology, National Poisons Information Service (London), Guy's and St. Thomas' Hospital, London, UK

³Consultant Physician and Clinical Toxicologist, National Poisons Information Service (London), Guy's and St. Thomas' Hospital, London, UK

Correspondence: David Wood, dwood@sghms.ac.uk

Received: 26 November 2002

Revisions requested: 18 December 2002

Revisions received: 3 January 2003

Accepted: 7 January 2003

Published: 6 March 2003

Critical Care 2003, **7**:147-154 (DOI 10.1186/cc1880)This article is online at <http://ccforum.com/content/7/2/147>

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Abstract

Background The number of patients awaiting allograft transplantation in the UK exceeds the number of organs offered for transplantation each year. Most organ donors tend to be young, fit and healthy individuals who die because of trauma or sudden cardiac arrest. Patients who die from drug and poison intoxication tend to have similar characteristics but are less frequently offered as potential organ donors.

Methods A postal questionnaire survey of all transplantation centres and an equal number of intensive care units in the UK was undertaken. The use of kidney, heart, lung, liver and pancreas transplants from poisoned patients following deliberate methanol ingestion, cardiac arrest presumed secondary to cocaine overdose, accidental domestic carbon monoxide inhalation and industrial cyanide exposure were used as case scenarios.

Results Response rates were 70% for transplantation centres and 50% for intensive care unit directors. Over 80% of organs would be offered or discussed with transplant coordinators by intensive care unit directors. Transplantation physicians/surgeons would consider transplanting organs in up to 100% of case scenarios, depending on the organ and poisoning or intoxication involved.

Discussion The postal survey presented here shows that most transplantation physicians and surgeons and intensive care unit directors would consider those who die following acute drug intoxication and poisoning as potential organ donors. The previously reported literature shows in general that transplanted organs from poisoned patients have good long-term survival, although the number of reports is small. Poisoned patients are another pool of organ donors who at present are probably underused by transplantation services.

Keywords brain stem death, drug intoxication, poisoning, questionnaire, transplantation

Introduction

In the UK, like in many countries, the number of individuals awaiting allograft organ transplantation exceeds the number of organs offered. In 2001, a total of 2339 allograft organ transplantations occurred but 5510 patients remained on the waiting list for transplantation, despite efforts to increase public awareness of organ donation through media campaigns [1].

The majority of donated allograft organs are offered from young, previously fit individuals who die because of trauma, sudden cardiac death or intracerebral catastrophes. Patients presenting to acute medical services after drug or poison intoxication usually survive with supportive care and poison-specific treatment, although a minority do not and are subsequently declared brain stem dead [2]. These patients represent a further pool of potential organ donors for those

on the transplantation waiting lists. However, currently it is estimated that fewer than 1% of all organ donors in Western Europe and the USA are from poisoned donors [3].

In the UK there are over 3200 deaths per year from poisoning; carbon monoxide is the leading single cause of fatal poisoning (688 deaths in 1999), with analgesics being the commonest drug group causing poisoning fatalities (1093 deaths in 1999, the majority [990] of which were opioid related), followed by antidepressants (353 deaths in 1999) [4]. The published data concerning these deaths [4] are not of sufficient detail to enable one to estimate the suitability of such poisoned individuals to act as organ donors (e.g. location of death [home versus hospital], cause of death [cardiac arrest versus brain death]). However, in our clinical experience a substantial proportion of these patients reach hospital alive, and they would therefore be expected to represent a potential group in which organ donation could be considered. The decision to offer and accept organs from poisoned patients is complicated both by the concern of declaring that patient brain stem dead and by the concern of potential injury to the recipient by the toxin involved.

There have been several case reports and case series of patients successfully being transplanted with organs from acutely poisoned patients. The major reports of transplantation following poisoning include series of 18 from Belgium (including seven from methanol-poisoned patients), 17 from the USA, 16 from Spain (all from methanol-poisoned donors) and eight from Spain (all from ecstasy-poisoned donors) [5–9]. The reports included poisonings with carbon monoxide, methanol, insulin, barbiturates, antidepressants and drugs of abuse. There has also been a report of six intrathoracic transplantations following carbon monoxide exposure in the UK [10]. Most of the organs transplanted were reported to have normal graft function at 6–12 months after transplantation. There have been reports of normally functioning hearts 6 years after carbon monoxide and 8 years after methanol poisoning [11,12]. There has only been one consensus report relating to paracetamol, barbiturate and carbon monoxide poisoned patients as potential organ donors for cardiac allograft transplantation [13]. That survey supported the use of poisoned patients and those with a history of drug abuse as potential organ donors, although there was not complete agreement among all heart surgeons on the suitability of the hearts offered. However, there have been no other published surveys on the acceptance of other organs for transplantation in other poisonings, and no surveys of intensive care units on whether poisoned individuals would be considered potential organ donors have been reported.

Method

Postal questionnaires were sent to transplant surgeons and/or physicians at all UK centres currently undertaking heart, lung, kidney, liver or pancreas transplantation. They were also sent to an equal number of directors of intensive

care units at hospitals not undertaking transplantations. The questionnaire consisted of four different scenarios involving brain stem death resulting from acute drug or poison intoxication. Minimal information was given in the scenarios concerning the medical condition of the patient and other factors that may be involved in the decision concerning transplantation, because the responses required related only to the specific poison involved. Summaries of the scenarios are as follows (see Appendix 1 for full case scenarios).

- Case 1: deliberate methanol ingestion, presenting 24 hours after ingestion and not responding to appropriate medical management.
- Case 2: known cocaine user found collapsed with a presumed cocaine overdose and an out-of-hospital cardiac arrest (no details concerning the route of drug use were given).
- Case 3: accidental carbon monoxide inhalation at home.
- Case 4: accidental industrial cyanide exposure.

In each case, respondents were asked whether they would accept or offer the organs for donation. Information concerning further investigations in organs accepted/offered and the reason(s) for refusal of organs was also sought.

Results

Survey forms were sent out to 67 doctors in the 30 transplantation centres in the UK (35 surgeons and 32 physicians involved in transplantation) and to 30 directors of intensive care units not currently undertaking transplantation. Following the initial mailing, nonresponders were sent a follow-up letter and a further survey form. Response rates were 52%, 70% and 50% for transplant surgeons/physicians, transplantation centres and intensive care unit directors, respectively.

Intensive care units

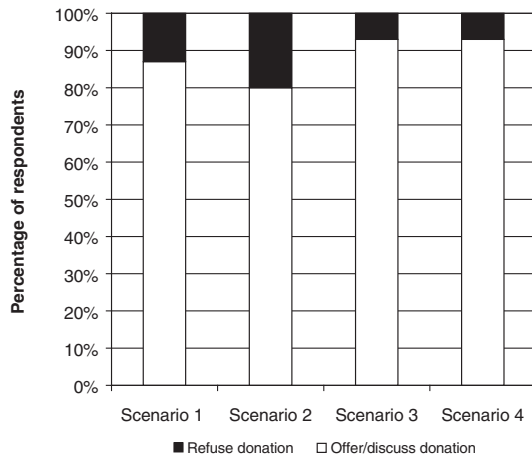
Replies from directors of intensive care units are shown in Fig. 1, which illustrates that most directors would offer poisoned patients as potential organ donors and leave the decision concerning organ harvesting to local transplantation team(s). Advice from toxicology services and transplantation coordinators would have been sought concerning further investigation(s) before organ harvesting.

Transplantation centres

Replies from transplant surgeons and physicians are shown in Fig. 2. These illustrate that, for each organ, more than 70% of those involved in transplantation would consider or accept patients who had been poisoned with methanol, cyanide or carbon monoxide as organ donors; however, only about 50% would consider or accept organs from patients who had been poisoned with cocaine.

Reasons for rejection

Although organs were rejected based on the case scenarios given, only 40% of the respondents gave reasons for refusal,

Figure 1

Responses from intensive care unit physicians to either offer/discuss or to refuse possible organ donation.

and this might not have related to all organs refused. In methanol poisoning, methanol-induced renal, pancreatic and liver damage, and treatment of alcohol-induced pancreatic damage were given as reasons for refusal. Following the out-of-hospital cardiac arrest and presumed cocaine ingestion, concerns were raised regarding possible undiagnosed HIV and viral hepatitis, because other drug ingestion and possible intravenous drug use was suspected. In this case, two respondents suggested use of such organs only in recipients with known HIV infection or in those classified as 'high need patients', with rapidly progressive underlying organ failure. Concern regarding hypoxia to heart, lungs and liver was raised following carbon monoxide exposure, and one respondent stated that they had previously encountered organ failure of a liver transplanted following carbon monoxide exposure of the donor. Similarly, cold ischaemic time following cyanide exposure was the main reason for refusal; one respondent was concerned about cyanide-induced renal and hepatic toxicity.

Additional investigations

Most respondents did not suggest any additional investigations other than those usually undertaken before organ harvesting and transplantation. Drug or toxin concentrations were requested by a small number of respondents for the methanol ($n=2$), carbon monoxide ($n=2$) and cyanide ($n=3$) exposures.

Discussion

The postal questionnaire survey reported here sought the opinions both on acceptance of organs for transplantation and on donation of such organs following acute drug and poison intoxication. In general, intensive care unit directors would consider or offer all organs following poisoning-related

deaths and, except those from patients at high risk for blood-borne viral infections, most would be accepted by transplantation teams.

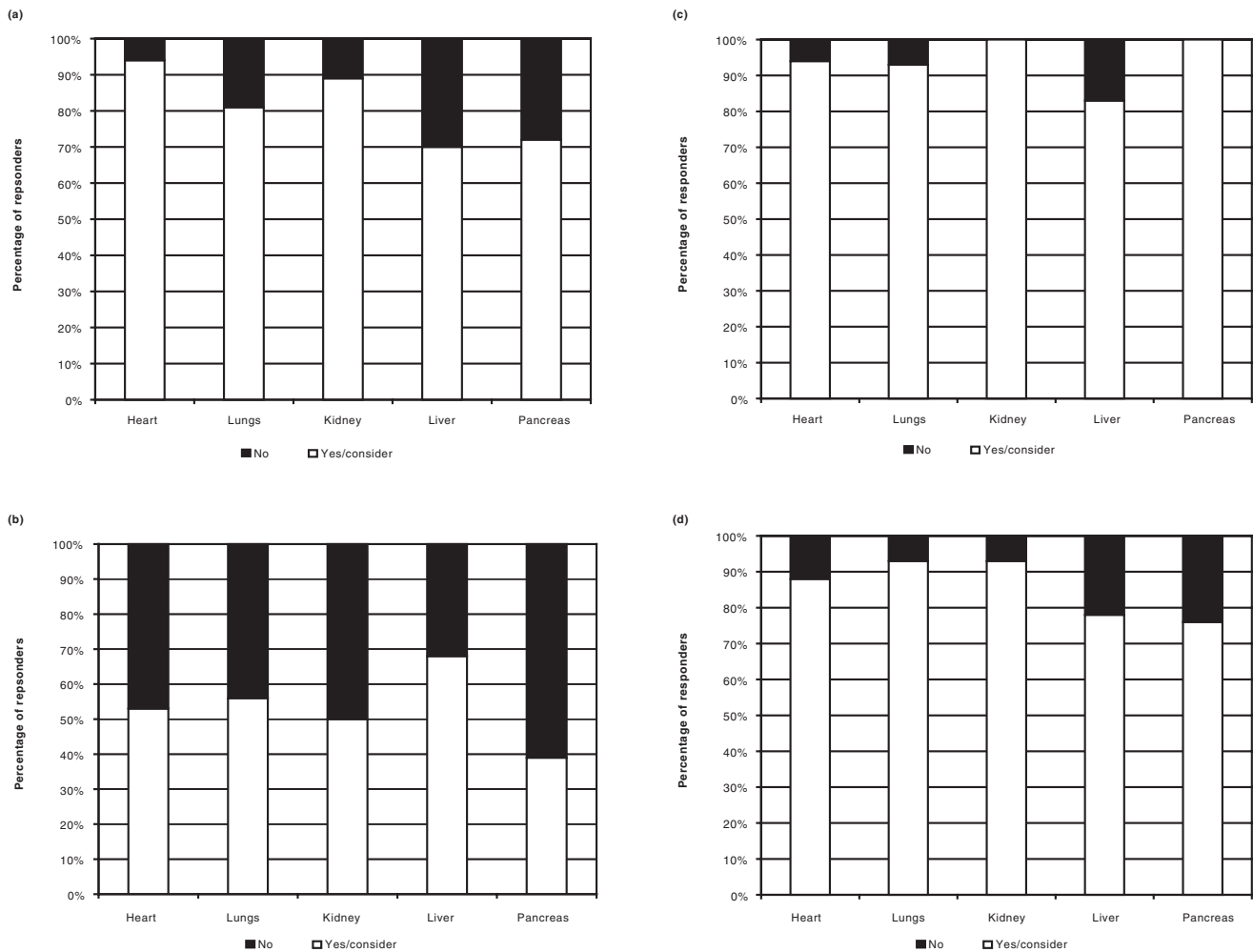
Investigations required by transplantation teams before accepting a poisoned patient's organ for donation are not clear. Simple measures of function such as liver and renal function, arterial blood gases or echocardiography may not sufficiently show toxin-related damage to the organ. The majority of respondents did not suggest any investigations other than those usually undertaken before accepting an organ for transplantation, such as liver and renal function tests, creatinine clearance, echocardiography, chest radiography, and serological testing for HIV and hepatitis. Only four respondents suggested measurement of cyanide concentrations in the case scenario of cyanide exposure, two suggested measurement of carboxy-haemoglobin concentrations in the carbon monoxide scenario, and one suggested measurement of methanol concentration in the methanol scenario. A few also suggested biopsies of the organ, but only in relation to liver and kidney transplantation. If there is any doubt in cases such as these, we would suggest liaison with clinical toxicologists at an early stage with a view to appropriate drug and toxin screening of the donor.

A further issue is accurate diagnosis of brain stem death in poisoned patients. In 1998 an Academy of the Royal College Working Party published a Code of Practice for diagnosis of brain stem death, which included guidelines for the management of potential organ and tissue donors [14]. In common with other guidelines on the diagnosis of brain stem death [15], this document states that it is important to exclude the presence of sedative drugs as a cause of central nervous system depression before the diagnosis of brain stem death. Drug levels following poisoning may be difficult to interpret because of altered toxicokinetics following poisonings that are different from the standard pharmacokinetics for a particular drug [16]. In many poisoned patients, therefore, the diagnosis of brain stem death will require an appropriate and accurate toxicology screen guided by a clinical toxicologist in order to exclude other drugs that might have been ingested by the patient and therapeutic agents that might have been given to the patient, such as benzodiazepines, opioids and barbiturates. Some authors also advocate the use of confirmatory radiological (e.g. magnetic resonance imaging/magnetic resonance angiography) [17] or electrophysiological (e.g. electroencephalography, evoked potentials) [3] measures, in addition to the standard clinical criteria, in the diagnosis of brain stem death.

Methanol

Methanol is rapidly absorbed from the gastrointestinal tract following ingestion and is metabolized by alcohol dehydrogenase to formate, which is responsible for the profound metabolic acidosis and ocular toxicity following ingestion [18]. However, ethylene glycol, through metabolism to oxalic, glycolic and

Figure 2



Response rates for consideration of organ transplantation after various poisonings from transplantation physicians/surgeons. **(a)** Methanol intoxication. **(b)** Cocaine intoxication. **(c)** Carbon monoxide. **(d)** Cyanide intoxication.

glyoxylic acids, not only produces a profound metabolic acidosis but also renal damage and hypocalcaemia [19]. The majority of patients who ingest methanol and ethylene glycol are successfully treated with an alcohol dehydrogenase inhibitor such as ethanol, often together with haemodialysis in severe poisoning, with no long-term effects [18,19].

Although the kidney is among the main organs of toxicity, the first reported successful transplantation following methanol ingestion showed long-term survival of four transplanted kidneys [20]. Subsequently, three case series of organ donation following methanol poisoning were reported [6,8,21]. The largest series involved a total of 38 transplanted organs (29 kidneys, four hearts and five livers) from 16 methanol-poisoned donors [8]. None of the recipients developed a metabolic acidosis or other features of methanol poisoning. There were two deaths (one liver and one heart recipient) from

acute rejection and one unrelated liver recipient death within the first month; the other 36 recipients were all discharged from hospital with normal graft function. At 1-year follow up, the three heart and three liver recipients, and 92.6% of the kidney recipients had normal graft function. These figures are comparable to the short-term and long-term outcomes from nonpoisoned donors in the same centres over this time period [8]. In another series, 13 kidneys, three livers, one heart and one bilateral lung were successfully transplanted from seven methanol-poisoned donors [6]. Follow up revealed normal organ function in all cases at 1 year, and two kidney recipients and the heart recipient had functioning grafts at 9 and 7 years after transplantation, respectively. These results are similar to those reported in a case series of five patients following methanol ingestion [21]. In that reported series four livers, 10 kidneys and one heart were transplanted, although the duration of long-term function was

not reported. One further heart recipient died during transplantation and one liver recipient died of unrelated sepsis.

Methanol and its metabolites have been reported to cause both elevated pancreatic enzymes and a pancreatitis, which suggests that successful pancreatic transplantation may not be possible [18]. To date there has only been one reported kidney–pancreas transplantation following methanol ingestion, with normal kidney and pancreas function at 10 months after transplantation [21]. Three further successful heart transplantations following methanol intoxication have been reported, although one recipient died at 18 months after transplantation from accelerated graft atherosclerosis [11].

In summary, there are a number of published cases of successful kidney, liver and heart transplantation, and one report of successful lung transplantation from methanol-poisoned patients with brain stem death, and we feel that these patients represent a suitable donor pool for transplantation. It is important that toxicological analyses be carried out in donors before transplantation in order to confirm that no methanol remains in the serum of the donors before organ harvesting.

Cocaine

Cocaine use is known to cause premature atherosclerotic disease, and therefore the cardiovascular system is the major site of organ-specific toxicity [22]. Despite this risk for atherosclerotic disease, most of the transplantation doctors we surveyed would consider using such individuals as potential heart donors.

Two successful liver transplantations following deaths related to cocaine ingestion have been reported [7]. One liver had impaired function before transplantation but this had improved by 10 days after transplantation, and both livers were functioning within normal limits at 1 year. These two donors and one other cocaine-related death provided six allograft renal transplantations. Although information was only available at 1-year follow up for four of those transplants, three were functioning within normal limits whereas the other had impaired function (elevated creatinine but functioning graft) [7]. There have been no published case reports of successful or unsuccessful heart, lung or pancreas transplantation following cocaine-related deaths.

In addition to the potential for early coronary artery disease, the other concern is the possibility of other drug use in a patient presenting with intoxication related to a drug of abuse. A careful detailed history would provide more information on the individual's previous and current drug use, but the accuracy of this is questionable and by the time patients are admitted to the intensive care unit it may be too late to obtain this information. It is therefore crucial that a detailed history regarding other drug use be taken early in the emergency department. Only in this case scenario did respondents suggest the use of organs only in those known already to be

HIV positive or in patients on the critical list for transplantation. There is the possibility of previous intravenous drug use, and therefore viral infections such as hepatitis B, hepatitis C and HIV, which could be transmitted to a potential donor, might be present. It is therefore important that all potential donors, particularly those with a history of intravenous drug use, undergo a viral screen to exclude HIV infection and hepatitis B/C carriage; however, even the most sensitive assays will not pick up donors who may still be in the window of infectivity [23].

Carbon monoxide

Carbon monoxide is the commonest single cause of fatal poisoning, and consequently there are more case reports and case series of transplantation following poisoning with carbon monoxide. It causes tissue hypoxia by having greater affinity for haemoglobin than oxygen, shifting the oxygen dissociation curve to the left and directly affecting mitochondria [24].

The first reported successful transplantation following carbon monoxide exposure was of a lung, with improving lung function tests and arterial blood gases at 8 months after transplantation [25]. The heart from this donor was unsuccessfully transplanted into another recipient, although the outcome was not reported. There has been only one other reported case of an initially successful lung transplantation, although the recipient died at 6 months from *Pneumocystis carinii* infection [10]. There have been more reports of kidney transplantation; renal function was reported as normal in six of the 14 recipient donors (information was unavailable on the remainder) [5,7,26]. These donor patients and two further carbon monoxide poisoned donors provided five successfully transplanted livers with normal long-term function [5,7,27]. There has also been one successfully transplanted pancreas, with normal blood glucose and C-peptide levels at long-term follow up [5].

There have been variable outcomes following heart transplantation from carbon monoxide poisoned donors. The first reported heart transplantation following carbon monoxide poisoning was unsuccessful, with the recipient dying on postoperative day 2 [24]. The first reported successful transplants to two recipients exhibited good long-term function, with ejection fractions of 56% and 59% 3 months after transplantation [28]. Two further unsuccessful transplantations were reported, with one recipient dying from postoperative shock [5] and the other from acute rejection [29], although there had been 9 months of good cardiac function. Following these conflicting reports, a consensus survey of UK heart transplantation surgeons was reported [13]. This showed that only 25% of surgeons thought that carbon monoxide poisoned patients would be suitable allograft heart donors. Following that consensus survey, a German heart transplantation unit reported on survival outcomes of five recipients transplanted over a 7-year period [30]. Three recipients died, one postoperatively from technical failure of the graft and overwhelm-

Table 1

Reported cases of toxins and poisons leading to successful organ transplantation following brain stem death

Organ transplanted	Poisons and toxins
Heart	Barbiturates, benzodiazepines, brodifacoum (rodenticide), carbon monoxide, cyanide, ecstasy, insulin, methanol, paracetamol, venlafaxine
Kidney	Barbiturates, benzodiazepines, brodifacoum, carbon monoxide, cocaine, cyanide, ecstasy, insulin, malathion, methanol, paracetamol, tricyclic antidepressants
Liver	<i>Amanita phalloides</i> mushroom, barbiturates, benzodiazepines, brodifacoum, carbon monoxide, cocaine, cyanide, ecstasy, lead, malathion, methaqualone, methanol, tricyclic antidepressants
Lung	Brodifacoum, carbon monoxide, ecstasy, methanol
Pancreas	Brodifacoum, carbon monoxide, cyanide, ecstasy, insulin methanol, paracetamol

ing sepsis following gut ischaemia, and the third from an undiagnosed pancreatic carcinoma at the time of the transplantation. Despite the negative opinion from the consensus survey on the use of carbon monoxide poisoned patients as organ donors and the German case series, there have been several reports of successful transplantation with good long-term outcome. Two successful heart transplantations were conducted in Canada following carbon monoxide exposure, although one patient died subsequently [11]. In the UK, five out of six patients transplanted were reported to have good long-term cardiac function, with one patient dying of multi-organ failure postoperatively [10].

In summary, there have been many reports of successful kidney transplantation and reports of successful pancreas, liver and lung transplantation from carbon monoxide poisoned donors. Heart transplantation from carbon monoxide poisoned donors remains a controversial issue, but 10 of the 17 reported cases had good long-term outcome. Because carbon monoxide is the commonest cause of poisoning fatalities and many of these deaths occur in young fit males [4], we feel that this group of patients represents an important and potentially underused donor pool.

Cyanide

Cyanide is rapidly absorbed through the skin and mucous membranes, and causes a chemical hypoxia by irreversibly inhibiting mitochondrial cytochrome oxidases. Cyanide poisoning is much less common than carbon monoxide poisoning, but fatalities still occur because tissues that are highly dependent on oxidative metabolism, such as brain and heart, are the most severely and rapidly damaged [31].

Despite the potential for severe cardiac toxicity, there have been two case reports of successful cardiac transplantation following cyanide exposure [32]. In the two recipients, cardiac function was reported as normal at 1 year and 8 months, respectively. Those donors also provided successful liver transplants, with normal liver function tests at follow up [32]. There have been more case reports of successful

kidney transplantation following cyanide poisoning [5,32–34]. The success and acceptance of kidneys for organ transplantation following cyanide exposure may reflect the increased ability of kidneys to withstand prolonged ischaemia and the lack of direct toxicity to kidney function from cyanide. Of 10 recipient patients, all had good long-term renal function after transplantation, except for one patient who decided to stop immunosuppressive therapy [33]. One patient also received a pancreas transplant at the same time as a kidney transplant [5]. At 1 year after transplantation, the recipient had normal fasting blood glucose and normal serum C-peptide levels.

Other poisonings

A series of eight organ transplantations (one heart, one bilateral lung, three kidney, one kidney–pancreas and two liver) from two ecstasy (3,4-methylenedioxymethamphetamine)-poisoned donors has been reported [9]. None of those recipients developed toxicity that could be related to ecstasy after transplantation. The bilateral lung recipient died from multi-organ failure secondary to sepsis 5 days after transplantation and one of the kidney recipients died from intestinal lymphoma at 6 months. All of the other recipients had normal graft function at follow up of between 7 and 53 months.

There have been individual case reports of organ donation following other poisonings: heart transplantation after a venlafaxine overdose [35]; liver and kidney transplantation after tricyclic antidepressant overdoses [5,36]; transplantation of multiple organs after insulin and barbiturate overdoses [5,7]; and liver transplantation after lead poisoning, although the recipient died intraoperatively from causes unrelated to organ function [7]. A full list of successful organ transplantations following self-poisonings is shown in Table 1. The consensus survey of UK heart transplant surgeons [13] also reported on opinions regarding barbiturate and paracetamol overdose and heart transplantation. In both poisonings, over 85% of surgeons would consider such organs suitable for transplantation. There has been one reported heart transplantation following a paracetamol poisoning (ejection fraction of 68% at 1 month) and one following barbiturate poisoning (ejection

Key messages

- The number of patients awaiting allograft transplantation in the UK exceeds the number of organs offered for transplantation
- Patients who die from drug and poison intoxication are not frequently considered as potential organ donors
- There are numerous reports of transplanted organs from poisoned patients with good long-term survival and organ function
- This survey of intensive care unit directors and transplantation teams shows that they would consider drug- and poison-related brain-stem death patients as potential drug donors
- Poisoned patients represent another pool of potential organ donors, and consideration of organ donation should be undertaken in all suitable cases

fraction of 82% at 1 year) [5]; liver donation from a paracetamol-poisoned donor would not be possible because the liver is the target organ for paracetamol toxicity. In addition, following barbiturate poisoning, there have been reports of successful kidney transplantation but also of two unsuccessful liver transplantations [5,7].

Conclusion

The postal survey presented here shows that most transplantation physicians and surgeons and intensive care unit directors would consider those who die following acute drug intoxication and poisoning as potential organ donors. In addition, directors of intensive care units, who make the initial suggestion of offering organs for transplantation, would refer all potentially suitable patients to the local transplantation teams. The previously reported literature shows in general that transplanted organs from poisoned patients have good long-term survival, although the number of reports is small. Poisoned patients represent another pool of organ donors that at present is probably underused by transplantation services.

Competing interests

None declared.

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Appendix 1: detailed case scenarios in the postal questionnaires

Case 1

A 35-year-old male patient presents to Accident and Emergency following deliberate ingestion of 150 ml methanol solution over 2 hours before. He is clinically drowsy and requires ventilatory support on intensive care. Despite aggressive medical management, he deteriorates and is declared brain dead.

Case 2

An 18-year-old known cocaine user is found collapsed in the street surrounded by several needles. He is successfully resuscitated after a presumed prolonged out-of-hospital arrest but he never regains consciousness. After 4 days on the intensive care unit, he is declared brain dead.

Case 3

A 35-year-old mother is found collapsed at home by a neighbour. She had recently had a new boiler system fitted, and it is believed that she has suffered significant carbon monoxide poisoning from the boiler and is declared brain dead in the intensive care unit.

Case 4

A 40-year-old cyanide worker is found collapsed by his work colleagues, having recently mixed chemicals at work. He is resuscitated by the workers' first aider and ambulance crew before transfer to hospital. He is managed on the intensive care unit but eventually is declared brain dead.