Transpl Int (1995) 8: 185–189

ORIGINAL ARTICLE

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Outcome following organ removal from poisoned donors: experience with 12 cases and a review of the literature

Received: 5 July 1994
Received after revision: 6 December 1994
Accepted: 2 January 1995

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Abstract From 1975 to 1993, our University Hospital performed 2789 graft procedures. During the same period, 12 poisoned, "brain-dead" patients were considered as organ donors. The toxic substances involved were: methaqualone ($n = 1$), benzodiazepine alone ($n = 1$), benzodiazepine plus tricyclic antidepressants ($n = 1$), tricyclic antidepressants alone ($n = 1$), barbiturates ($n = 2$), insulin ($n = 2$), carbon monoxide ($n = 1$), cyanide ($n = 1$), methanol ($n = 1$), and acetaminophen ($n = 1$). From these intoxicated persons, 32 organ transplants were obtained, but only 23 could be followed for 1 month and only 20 for 1 year. The outcome at 1 month was favorable in 20 of the 23 patients. Two heart transplant patients died within 24 h after grafting from stroke and acute heart failure, respectively. Preoperative hepatic encephalopathy was not corrected after grafting and was directly responsible for the death of a liver transplant patient. After 1 year, 15 of the 20 recipients were still alive. Chronic hepatic graft rejection led to a fatal outcome in one recipient and to second grafting in another. Finally, one recipient died from delayed neoplasia. Based on our experience, organ procurement may be considered in a few select cases of acute poisoning. Attention should, however, be drawn to possible graft damage due to some poisons.

Key words Poisoning, organ donation · Organ donation, poisoning · Brain death, poisoning

Introduction

The mortality rate due to acute poisoning is currently low and mainly related to lesional toxins that may irreversibly affect cell integrity (e.g., paraquat, colchicine). With toxic substances that cause only temporary cell damage, tissue hypoxia is often the consequence of unsuccessful resuscitation after prolonged cardiocirculatory arrest. "Brain death" may, in some instances, be the ultimate manifestation of this damage. Little data about organ procurement from brain-dead victims of acute poisoning has been published [9]. We report our experience transplanting organs from brain-dead, poisoned donors.

Materials and methods

Between January 1975 and December 1993, our University Hospital (900 beds) performed 2789 graft procedures (1922 kidneys, 623 livers, 141 hearts, and 43 pancreases). During the same period, 1174 patients were admitted to the Intensive Care Unit (ICU) for acute poisoning, and (1.9%) had a fatal outcome. Only 12 of them were considered as potential organ donors after evidence of brain death, according to the Belgian "presumed consent" law. These 12 donors provided organs for 32 recipients, but only 23 could be followed at 1 month and 20 at 1 year. (The 1-year follow-up is not yet available for the most recently transplanted grafts – heart and kidneys – coming from the acetaminophen-poisoned donor.) The toxic substances and organs removed are listed in table 1.

Some of the donor exclusion criteria are related to the nature of the toxic substance and others to the clinical condition of the donor. The heart was not removed from the two patients with tricy-

Table 1 Toxic substances and organs removed [*BZD* benzodiazepine, *TCA* tricyclic antidepressant, *X* organ grafted, *(X)* organ grafted but lack of further information, *0* no compatible recipient or no experience]

Toxic substances	Right kidney (n = 11)	Left kidney (n = 11)	Heart (n = 5)	Liver (n = 5)	Pancreas (n = 2)
Methaqualone	0	0	0	X	0
BZD	X	(X)	X	X	0
BZD + TCA	(X)	X	Valves		
TCA	X	(X)			0
Barbiturates	(X)	X		(X)	0
Barbiturates	(X)	(X)	X	X	0
Insulin	(X)	X	X		Islet cells
Insulin	(X)	X	Valves		
Carbon monoxide	X	X	X	X	X
Cyanide	X	X			X
Methanol	X	X			
Acetaminophen	X	X	X		Islet cells

Table 2 Outcome of the kidney transplant patients (*BZD* benzodiazepines, *TCA* tricyclic antidepressants)

Kidney			
Toxic substances	Outcome (1 month)	Outcome (1 year)	Events
	Serum creatinine (mg/dl) (normal 0.8–1.3)	Serum creatinine (mg/dl) (normal 0.8–1.3)	
BZD	1.37	1.36	
BZD + TCA	1.2	2.1	
TCA	1.1	5	Chronic rejection
Barbiturates	1.29	0.95	
Insulin	1.36	1.43	
Insulin	0.9	[a]	Bladder carcinoma
Carbon monoxide	1.31 1.07	1.2 0.91	
Cyanide	1.12 1.16	1.25 1.2	
Methanol	1.49 1.5	1.46 1.25	
Acetaminophen	2.1 1.7	[b] [b]	

[a] Death
[b] Recent observation

clic antidepressant (TCA) poisoning. This was also the case when high doses of inotropic agents were required following barbiturate ($n = 1$), insulin ($n = 1$), and cyanide ($n = 1$) poisoning. Furthermore, the electrocardiogram had disclosed a Wolff-Parkinson-White syndrome in the cyanide-poisoned donor. Finally, the previous use (8 years before) of adriamycine for an ovarian cancer, together with the nature of the toxic substance, excluded heart donation in the methanol-poisoned patient. The liver was not removed from a TCA-poisoned patient with a long ICU stay. Sustained hypotension with probable ischemic liver damage was noted in two other patients with TCA or insulin poisoning. Hypernatremia and abnormal liver function tests were present in two cases of insulin or cyanide poisoning. Previous abdominal radiotherapy excluded the removal of the liver and pancreas from the methanol-intoxicated donor. Finally, in the methaqualone-poisoned donor, kidney, heart, and pancreas were excluded for logistical problems (absence of compatible recipients for the kidneys, lack of experience on the part of our surgical team in heart and pancreas transplantation at that time).

Results

Of the 23 recipients, 20 (85 %) survived 1 month, and 15 of the 20 (75 %) survived 1 year. These data can be further analyzed with respect to the organs grafted.

Kidney grafts (Table 2)

The immediate outcome (at 1 month) was favorable in all of the recipients, with serum creatinine values within the normal range. At 1 year, the survival rate was 93 %. One recipient died from metastatic bladder carcinoma, and another developed chronic kidney rejection (with serum creatinine values higher than 5 mg/dl).

Heart grafts (Table 3)

Among heart transplant patients, one recipient died within the first 24 h as a result of a stroke. A second died 7 h after grafting from heart failure. The survival rate was thus 60 % at 1 month. The indication for heart transplantation was a terminal ischemic cardiopathy in the latter case and the patient was in very poor physical condition at the beginning of the transplantation (shock, lactic acidosis, pulmonary hypertension, acute renal failure). The survival rate at 1 year was 50 %, with normal cardiac function assessed by echocardiography in all patients.

Table 3 Outcome of the heart transplant patients (*EF* ejection fraction)

Heart			
Toxic substances	Outcome (1 month)	Outcome (1 year)	Events
	echocardiography EF %	echocardiography EF %	
BZD	[a]		Stroke
Barbiturates	50	82	
Insulin	89	72	
Carbon monoxide	[a]		Preoperative shock
Acetaminophen	68	[b]	

[a] Death
[b] Recent observation

Table 4 Outcome of the liver transplant patients [*LFT* liver function tests (enzymes, bilirubin, prothrobin time)]

Liver			
Toxic substances	Outcome (1 month)	Outcome (1 year)	Events
	LFT	LFT	
Methaqualone	[a]		Preoperative encephalopathy
BZD	Normal	Normal	
Barbiturates	Normal	[a]	Chronic rejection
Carbon monoxide	Normal	Normal	Second graft

[a] Death

Table 5 Outcome of the pancreas transplant patients

Pancreas			
Toxic substances	Outcome (1 month)	Outcome (1 year)	Events
	Serum C-peptide (μg/l) (normal 1–2.5)	Serum C-peptide (μg/l) (normal 1–2.5)	
Carbon monoxide	1.5	0.77	
Cyanide	0.75	1.5	

Liver grafts (Table 4)

In the liver group, one recipient died 5 days post-transplantation from pre-existing encephalopathy, resulting in a 75 % survival rate at 1 month. At 1 year, two of four recipients were still alive (50 % survival), as a recipient died 8 months after transplantation from chronic liver rejection. Regrafting was required in another recipient for the same reason. The two remaining recipients had normal liver function tests.

Pancreas grafts (Table 5)

The two pancreas recipients had an uneventful follow-up at 1 month and 1 year (normal fasting glucose blood level and serum C-peptide). Pancreas grafting was combined with successful kidney grafting in both patients. Islet cells were stored in a graft bank in two cases.

Discussion

Due to the low mortality rate following acute poisoning, brain death is rare and often related to hypoxic lesions after cardiopulmonary resuscitation, in the absence of direct brain damage due to the toxic substance. As we observed, some agents may act mainly as functional toxins, temporarily impairing cellular functions and causing various systemic manifestations. The brain is probably the organ that is most susceptible to metabolic dysfunction, and irreversible brain damage may occur while the other organs continue to work normally for some time after exposure to the poison, provided there is adequate supportive therapy.

Cyanide is a good example of a functional toxic substance. Cyanide interacts with cellular respiration, inducing an acute metabolic acidosis associated with vasoplegic shock, cardiac incompetence, and a drastic reduction in the D(a-v)O2 [14]. The nerve cells, which are particularly sensitive to hypoxia, are damaged first, leading to brain death. We previously described successful renal and combined renal-pancreatic transplantations after acute cyanide poisoning [6, 16]. The organs were removed 44 h after poisoning when the donor had normal hemodynamic values and low arterial lactate values (< 1 mmol/l). Cyanide blood levels were 1.8 μmol/l at this time, and it is generally accepted that levels of less than 7 μmol/l do not cause any symptoms [5]. Heart, liver, skin, cornea, and bone grafts were also reported from victims of cyanide poisoning [2, 10, 15]. As for the specific treatment, correction of metabolic acidosis, optimal oxygenation (ventilation with 100 % oxygen), and maintenance of hemodynamic stability are mandatory. The antidotal therapy (supratherapeutic doses of hydroxocobalamine and sodium hyposulfite) probably helps to restore hemodynamics [12].

Carbon monoxide, like cyanide, primarily affects the tissues most sensitive to oxygen deprivation, particularly the central nervous system and the myocardium. Measurement of the blood carboxyhemoglobin level does not reflect the tissue level of carbon monoxide [4]. In our study, we had one case of carbon monoxide poisoning, and several organs were procured from this patient. At the time of brain death, the serum creatinine concentration was normal (1.05 mg/dl); previous lactic acidosis and hypernatremia were corrected. Liver biopsy and echocardiography were also normal. The out-

come of the double renal-pancreatic transplantation was favorable and graft function remained within the normal range when it was assayed 72 months after the transplantation. The heart transplant patient died 7 h after grafting. Severe preoperative lactacidemia was present and hemodynamic values could not be improved after grafting. The grafted liver worked immediately; however a second transplantation was required for chronic rejection.

Hebert et al. published two cases of renal transplantation after a carbon monoxide suicide attempt [7]. The graft functioned well in the first patient; the second patient needed transient hemodialysis (7 days) because of acute tubular necrosis and acute rejection. The outcome at 20 months was favorable in both cases, with normal serum creatinine values. Kidneys are probably more resistant than other organs to the hypoxia induced by such intoxication. Transient proteinuria may be seen in the first hours after carbon monoxide poisoning, but this does not preclude organ removal, provided the renal function is adequate at the time of removal [1, 7]. No data have been published about pancreas and liver transplantation, and further information is needed. From our experience, it is difficult to correlate the rejection of the liver transplant with the nature of the toxic product; the favorable outcome of the double renal-pancreatic transplantation suggests that both organs may be considered in such a poisoning.

By contrast, Karwande et al. reported an unsuccessful heart transplantation after smoke inhalation [8]. Although the poisoned victim recovered after prolonged cardiorespiratory arrest, he developed irreversible brain lesions. Echocardiography was normal and electrocardiogram showed only diffuse, nonspecific ST segment changes. The recipient died from progressive, global cardiac failure 4 days post-transplantation. The autopsy of the transplanted heart revealed multiple confluent endocardial hemorrhages, most prominent in the left ventricle and papillary muscles. Microscopic findings included global coagulative necrosis and diffuse fatty infiltration of the myocytes. Immunofluorescence showed that humoral-mediated graft rejection had not occurred. These findings clearly suggest that the heart from a carbon monoxide-intoxicated person should not be used for transplantation. A normal echocardiography and the absence of electrocardiographic changes do not rule out significant myocardial damage.

An insulin overdose is often accompanied by irreversible brain damage. After brain death, there is probably no contraindication to organ removal in the absence of any demonstrable dysfunction.

Methanol produces a well-recognized clinical picture that is a contraindication to the removal of the liver and pancreas. After oral poisoning, a transient but severe cardiac failure, associated with EKG changes (blocks and T wave abnormalities), develops rapidly [3]. Cardiac dilatation and myocyte degeneration have been described in intoxicated animals [13]. These lesions are contraindications to heart donation. Our favorable experience in a case of double renal transplantation after massive methanol ingestion (both patients are still alive with normal renal function more than 10 years after the procedure) allows us to propose kidneys for organ procurement in some cases.

Acetaminophen poisoning causes centrolobular liver necrosis, acute proximal renal tubular necrosis, and diffuse alveolar pulmonary damage. In 1991, Price et al. described a case of heart transplantation after a fatal acetaminophen overdose; the recipient died 14 days after the procedure from sepsis, but the autopsy of the transplanted heart showed extensive subendocardial myocyte necrosis related to drug toxicity and no rejection [11]. These observations are also a contraindication to organ removal in the case of paracetamol poisoning, although we have recently used the heart and kidney in such a case.

For other substances, such as tricyclic antidepressants, antalgic drugs (dextropropoxyphene, opiates), and solvents (perchlorethylene, ethylene glycol), further information is needed.

In conclusion, we report 23 grafting procedures from 12 poisoned donors. The immediate outcome was favorable in 85 % of the cases. One year later, 75 % of the recipients were still alive. These results are similar to those observed in a population of nontoxic, brain-dead donors. Our observations illustrate the fact that organ procurement may be considered in a few select cases of acute poisoning, yet, general and toxic-related criteria have to be taken into account. In the future, the analysis of toxicokinetics and tissue concentrations should guide the decision of whether or not to remove organs.

References

1. Bessoudo R, Gray J (1978) Carbon monoxide poisoning and nonoliguric acute renal failure. Can Med Assoc J 19: 41–44
2. Brown PWG, Buckels JAC, Jain AB, McMaster P (1987) Successful cadaveric renal transplantation from a donor who died of cyanide poisoning. BMJ 294: 1325
3. Cavalli A, Volpi A, Maggioni AP, Tusa M, De Pieri G (1987) Severe reversible cardiac failure associated with methanol intoxication. Postgrad Med J 63: 867–868
4. Dolan MC (1985) Carbon monoxide poisoning. Can Med Assoc J 133: 539–542
5. Graham DL, Laman D, Theodore J, Robin E (1977) Acute cyanide poisoning complicated by lactic acidosis and pulmonary oedema. Arch Intern Med 137: 1051–1055

6. Hantson PE, Squifflet JP, Vekemans MC, Evrard P, Hassoun A, Sepulchre MA, De Ceuninck P, Mahieu P (1991) Successful pancreas and renal transplantations from a donor who died of cyanide poisoning. Clin Transplant 5: 419–421
7. Hebert MJ, Boucher A, Beaucage G, Girard R, Dandavino R (1992) Transplantation of kidneys from a donor with carbon monoxide poisoning. N Engl J Med 326: 1571
8. Karwande SV, Hopfenbeck JA, Renlund DG, Burton NA, Gay WA (1989) The Utah Transplantation Program. An avoidable pitfall in donor selection for heart transplantation. J Heart Transplant 8: 422–424
9. Leikin JB, Heyn-Lamb R, Aks S, Erickson T (1993) The toxic patient as a potential organ donor: one year follow-up (abstract). Vet Hum Toxicol 35: 318
10. Lindqvist TD, Oiland D, Weber K (1988) Cyanide poisoning victims as corneal transplant donors. Am J Ophthalmol 106: 354–355
11. Price IM, Poklis A, Johnson DE (1991) Fatal acetaminophen poisoning with evidence of subendocardial necrosis of the heart. J Forensic Sci 36: 930–935
12. Riou B, Gerard JL, La Rochelle CD, Bourdon R, Berdeaux A, Giudicelli JF (1991) Hemodynamic effects of hydroxocobalamin in conscious dogs. Anesthesiology 74: 552–558
13. Rowe VK, McCollister SB (1982) Alcohols. In: Clayton GD, Clayton FE (eds) Patty's industrial hygiene and toxicology. John Wiley & Sons, New York, pp 4557–4708
14. Singh BM, Coles N, Lewis P, Braithwaite RA, Nathrass M, Fitzgerald MG (1989) The metabolic effects of fatal cyanide poisoning. Postgrad Med J 65: 923–925
15. Swanson-Biearman S, Krenzelok EP, Snyder JW, Unkle DW, Nathan HM, Yang S-L (1993) Successful donation and transplantation of multiple organs from a victim of cyanide poisoning. Clin Toxicol 31: 95–99
16. Vekemans MC, Hantson PE, Fievez P, Gautier PE, Squifflet JP, Sepulchre MA, Hassoun A, De Ceuninck P, Mahieu P (1990) Cyanide as a functional poison: possibility of organ donation after brain death. Proceedings of the International Toxicology, Poison Control and Analytical Toxicology Bulletin de la Société des Sciences Medicales du Grand - Duché de Luxembourg, LUX TOX 198, pp 198–201