Commentary

Drug abusers and poisoned patients: a potential source of organs for transplantation?

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Summary

One of the major constraints to transplantation of solid organs is lack of availability of grafts and any attempt to use all available donors is to be welcomed. We address the possibility of expanding the transplant donor pool by inclusion of more patients who have suffered intoxication with drugs pre-mortem. Particularly important in this context is the exclusion of organ-specific damage, and also infective risk to the potential recipient due to viral causes.

Organ donation and successful retrieval of life-saving organs is a complex process involving co-ordination of multiple transplant teams. Current evidence indicates that the demand for organs continues to outstrip supply. Traditionally, organs have been donated from fit, young individuals who have died as a result of trauma. People who use drugs of abuse or who are self-poisoned are also young, yet only 37 of this group of individuals have been reported in the world-wide literature to have successfully acted as organ donors, the major reports including 12 patients in Belgium and 17 in the United States. They have included those poisoned by tricyclic antidepressant drugs, benzodiazepines, barbiturates, insulin, carbon monoxide, lead, cyanide, cocaine, methanol, paracetamol and multiple drugs, including amphetamines. Experience indicates that selected organs from such donors function as well in recipients as those from more conventional sources, as predicted by knowledge of the target organs or injury and avoidance of these (Table 1). The only exception has been two cases of cardiac transplantation following carbon monoxide poisoning or smoke inhalation, respectively. A recent survey of heart transplant surgeons in the UK revealed the majority believed that use of hearts from individuals with brain death caused by paracetamol or barbiturates should not be discouraged.

More than 327 deaths were reported due to poisoning in Scotland (from carbon monoxide to amitriptyline) according to the Registrar General’s figure for 1995. One would anticipate that a substantial number of these reached hospital alive initially, with the exception of perhaps opiate deaths in the community, due to the rapidity of onset of fatal sequelae. Even if only half of those reaching hospital could be used as organ donors, this would considerably expand the organ donor pool. Yet in 1994, none of these patients were used as organ donors (personal communication, Rosanne Bates, Scottish Liver Transplant Unit). So why are they not used more often and what can be done to improve this situation?

It may be that the lack of poisoned donors reflects difficulty in the diagnosis of brain death in the presence of drugs. Many criteria state that brain death cannot be diagnosed in the presence of drugs that mask central nervous system activity. There is a rule of thumb, based on the pharmacological principle that most drugs need five half-lives to be...
Table 1  Common drugs taken in overdosage and organ-specific toxicity, indicating other organs that may be suitable for transplantation

<table>
<thead>
<tr>
<th>Drugs</th>
<th>Organ-specific toxicity</th>
<th>Organs that may be suitable for transplantation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benzodiazepines (though</td>
<td>Central nervous system</td>
<td>Lung, heart, cornea, liver, kidney</td>
</tr>
<tr>
<td>benzodiazepines alone are</td>
<td>Central nervous system</td>
<td>All organs except pancreas; caution</td>
</tr>
<tr>
<td>unlikely to cause death)</td>
<td>Central nervous system</td>
<td>to avoid hypoglycaemia in the post-operative state</td>
</tr>
<tr>
<td>Insulin</td>
<td>Central nervous system, cardiovascular system</td>
<td>Liver, kidney, lungs</td>
</tr>
<tr>
<td>Tricyclic antidepressant</td>
<td>Central nervous system, cardiovascular system</td>
<td>Kidney, liver</td>
</tr>
<tr>
<td>drugs</td>
<td>Central nervous system, cardiovascular system</td>
<td>Lungs, liver, kidney</td>
</tr>
<tr>
<td>Carbon monoxide</td>
<td>Central nervous system, cardiovascular system</td>
<td>Heart, lungs</td>
</tr>
<tr>
<td>Cocaine</td>
<td>Central nervous system, liver, kidney</td>
<td>Lung, liver (if hepatic damage excluded), kidney</td>
</tr>
<tr>
<td>Methanol</td>
<td>Central nervous system, liver, kidney</td>
<td>Heart, lungs</td>
</tr>
<tr>
<td>Amphetamines</td>
<td>Central nervous system, cardiovascular system</td>
<td>Lung, liver</td>
</tr>
<tr>
<td>Paracetamol</td>
<td>Central nervous system, liver, kidney, often</td>
<td>Cornea, heart</td>
</tr>
<tr>
<td></td>
<td>secondary damage to lungs</td>
<td></td>
</tr>
</tbody>
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effectively eliminated from the circulation, to allow four half-lives of a drug before declaring death\textsuperscript{10} or to allow 2–3 days for drug effects to wear off,\textsuperscript{11} but whether this is satisfactory for seriously poisoned patients with saturated enzyme systems still remains to be evaluated, i.e. toxicokinetics may be very different from pharmacokinetics. The difficulties in diagnosing brain death in the presence of drugs could be improved if national guidelines were to be developed jointly between intensivists, transplant physicians, transplant surgeons and clinical toxicologists.

Such guidelines should also include the requirement for appropriate toxicological screening of potential donors. Intensive care doctors currently routinely take a history of drug use or abuse from relatives, and send a blood or urine sample to the laboratory for analysis. However, such samples should really be collected in the emergency department before transfer of the patient to ITU, and especially before the administration of any therapeutic drugs, as sedative agents will complicate the interpretation of screen assays. Guidelines on interpretation of ‘drug screens’ are also required, as most, for example, do not detect lysergic acid (LSD) or ethanol and are rarely the ‘screens’ that doctors suppose. Urine concentrations of drug are very poorly correlated with the amount ingested.\textsuperscript{9} Even plasma or serum concentrations may be difficult to interpret, as there may be up to a fourfold difference in the toxicodynamic effect of any given blood concentration of a drug, dependent on its distribution, cerebral blood flow and other factors.\textsuperscript{12} We would therefore recommend the involvement of clinical toxicologists in the National Poisons Information Service Centres in the UK in the diagnosis of brain death in the presence of drugs and also in interpreting the laboratory measurements, as they have expertise both in toxicokinetics and toxicodynamics.

The next problem for doctors considering use of poisoned patients as donors is whether the organs from the donor are fit for transplantation. Often simple blood tests such as liver function tests or serum creatinine estimations are not sufficiently sensitive for detecting injury of an organ which may be considered for transplantation. There is therefore likely to be a need to assess the extent of organ damage more directly, for example, by pre-transplant biopsy of the liver.

It is also particularly important, particularly in the drug abuse population, that all potential donors should undergo a thorough infectious disease screening prior to transplantation to exclude as far as possible the transmission of an infective agent such as hepatitis B or C (by second generation ELISA) or HIV by serological testing.\textsuperscript{13,14} In populations where hepatitis B and C are of low prevalence, such as in the UK, organs from patients who are serologically positive for these agents are routinely not used for transplantation purposes. There are guidelines now available on the use of organs from virally-infected individuals. Hepatitis C virus (HCV) infection in the organ donor and/or in the blood transfused in the peri-transplant period may be transmitted to the recipient.\textsuperscript{15} The natural history of HCV infection in the
immunosuppressed allograft recipient, and its impact on long-term patient outcome, are still being evaluated. However, although post-transplantation HCV infection is generally considered to be much less devastating than post-transplantation hepatitis B virus (HBV) infection, HCV even in the non-liver transplant patient may lead to cirrhosis.\textsuperscript{15} Approximately one-third of patients who received a kidney from a HCV carrier donor developed chronic rises in transaminases, and 56\% converted from HCV-RNA-negative to positive in the post-transplant period.\textsuperscript{16} An extended perfusion technique was shown to reduce the viral load in the kidney by 99\% and it is hoped that similar and newer techniques will increase the safety of organ donation in future.\textsuperscript{16}

However, a potentially transmissible viral infection in a donor may not preclude transplantation of organs into recipients with the same infection. This is particularly the case with cytomegalovirus infection since approximately 50\% of donors and recipients in the UK are positive. There is a 1 in 4 chance that a cytomegalovirus-negative recipient will receive a cytomegalovirus-positive organ. In such circumstances, the chances of serious cytomegalovirus infection in immunosuppressed patients are at least 55–60\%,\textsuperscript{17} though these may be reduced by early administration of gancyclovir.\textsuperscript{18,19} Early detection of cytomegalovirus infection in the host has important implications for post-transplant management,\textsuperscript{20,21} as it remains a major cause of problems following solid organ transplantation.\textsuperscript{22}

It is also important to identify which organs act as reservoirs for drugs\textsuperscript{23} and either not consider transplanting such organs, for example, a liver from a paracetamol poisoned patient, or take prophylactic measures such as administration of N-acetylcysteine in the case of donation of a heart from a paracetamol-poisoned patient.\textsuperscript{24}

The costs of having expanded donor criteria would probably be minimal (20\% more per organ has been estimated for using older, hypertensive or diabetic donors).\textsuperscript{25} There is, however, an interesting ethical dilemma of whether you tell the recipient that organ was from a self-poisoned patient or even a drug abuser. Our advice is that the patient should be fully appraised of the situation.

In summary, we believe that selected patients with drug-related deaths could and should be considered for donation to the transplantation programme using predetermined national criteria. This would increase the availability of organs to the UK transplant programmes. The accuracy of the diagnosis of irreversible brain damage, and understanding of the toxicokinetic and toxicodynamic properties of the drugs involved, are essential in this setting. Equally important is the exclusion of infective risk to the potential recipient due to viral causes in the donor.

References

of CMV in solid organ recipients: what is the predictive value for the development of disease and should PCR be used to guide antiviral therapy? Transplantation 1997; 63: 275–9.

