Utilisation of kidneys from deceased donors at increased risk of infectious disease transmission: a step in the right direction

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Introduction

Renal transplantation is acknowledged as the gold standard therapy for children with end-stage kidney disease (ESKD), resulting in improved survival, better growth, and more favourable social outcomes when compared with remaining on dialysis [1, 2]. A kidney from a living donor is the best option for these children due to a shorter waiting time and better short- and long-term graft function and survival than receiving a kidney from a deceased donor [3, 4]. However, prioritising children for deceased donor renal transplantation resulting in shorter waiting times is leading to some centres reducing their living donor rates [5]. A degree of uncertainty is another drawback to deceased donor kidney transplantation; a history cannot be taken from a deceased patient and few of us tell our loved ones every detail of our medical history or social behaviours. This is especially relevant when we attempt to quantify the risk of transmission of serious blood-borne viruses (BBV), such as human immunodeficiency virus (HIV), hepatitis B virus (HBV) and hepatitis C virus (HCV), from a deceased donor.

Donors with increased risk for disease transmission

Hwang et al. report on the experience of transplanting kidneys from deceased donors at increased risk of BBV disease

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transmission into paediatric recipients in the United States of America (USA) [6]. These donor risk factors include sexual practices associated with increased risk, illicit use of injectable drugs, and incarceration. Such donors in the USA are designated as being of increased risk for disease transmission (IRD), with specific focus on risk factors for HIV, HBV and HCV. This national study from 2004 to 2017 demonstrated excellent patient and renal allograft outcomes in 473 children who received kidney-only transplants from IRD donors with no apparent cases of viral transmission of HIV, HBV or HCV. The authors calculated that improved utilisation of IRD donors could significantly increase paediatric kidney transplant rates in the USA. However, transplant clinicians need to carefully consider whether they should accept these organs from IRD donors and if this should become their normal practice in 2019. For those who are less risk averse, transplant clinicians should consider what information should be given to the proposed paediatric recipient and family at the time of listing for deceased donor renal transplantation as well as at the time of organ donor offer with IRD. Transplant clinicians should be aware of their updated local facilities for testing in prospective paediatric recipients and what treatments are available to those paediatric recipients who develop BBV after transplantation of organs from donors with IRD.

This study will provide encouragement to paediatric transplant teams considering implanting kidneys from deceased donors without serological evidence of BBV infection but with increased risk behaviours. However, this is a complex field, and transplant clinicians must be aware of other important issues discussed in this manuscript.

Differences in IRD donors and transmission risks

It is unclear how generalisable these findings are outside of the USA as IRD donors make up a relatively large (and increasing) proportion of the deceased donor population in the USA [7], at

least partly due to an epidemic of opioid use [8]. Deceased donors with a history of drug overdose are far more common in the USA than Australia and New Zealand or the UK with rates of 9.3% versus 2.7% and 0.3%, respectively [9].

In addition, when comparing utilisation rates of IRD donors, it is imperative to consider what the underlying prevalence of BBV in the population. Estimated prevalence of HIV in intravenous drug user (IVDU) populations are 3.6%, 1.7%, 1.3% and 0.2% in the USA, New Zealand, Australia and the UK, respectively. Estimated prevalence data of HCV in IVDU populations are 73%, 57%, 57% and 50% in the USA, New Zealand, Australia and the UK, respectively [9].

Nucleic acid testing

Given the relatively common frequency of IVDU donors in the USA, it is understandable that nucleic acid testing (NAT) for HIV, HBV and HCV is mandatory for those deceased donors identified as IRD. NAT tests, which detect viral DNA or RNA, significantly shorten the ‘window period’, which is the duration between exposure to an infectious agent and detection in the infected individual’s blood, when compared with serology. Window periods for HIV and HCV are approximately 5 to 9 days for NAT tests, but 1 to 2 months for antibody-based serological tests [10, 11]. We assume that the IRD donors in Hwang’s analysis were both NAT negative and serologically negative. However, NAT tests are not available prior to organ offering in every country.

The availability of NAT testing, the relatively high prevalence of IVDU and recent concerns about the access of children with ESKD to deceased donor kidneys in the USA [12] combine to make the use of IRD donors a more feasible option to patients, families and clinicians. Declining a kidney from an IRD donor prolongs median waiting time by 9.6 months (11.2 months among those under 6 years of age and 8.8 months among those on dialysis) [13]. These drivers may not be present in other countries, specifically, those countries with short waiting times for deceased donor kidney transplantation in Europe [14].

Risk according to exposure timing

There may be some degree of selection bias evident in this study. The timing of exposure to an infectious agent is important in deciding whether to accept or decline the offer of a kidney from an IRD donor. The risks of disease transmission from a NAT-negative donor with a history of IVDU found in respiratory arrest with a needle in their arm will be significantly higher than the risks associated with a NAT-negative donor who was in prison 11 months ago, although both will be classified as IRD donors [10, 11]. There are no detailed data on

donor risk behaviours leading to IRD classification in this manuscript, although the proportion of donors with IVDU or anoxic brain injury was higher in the IRD group than the non-IRD group [6]. This makes it difficult to accurately characterise the residual risk of viral transmission in this donor group that is likely to be heterogeneous with respect to risk behaviour; this is especially relevant given that the national criteria for identification of IRD donors changed during the study period.

Educational tools

It is essential that transplant centres that accept organs from IRD donors carefully consider the best way to educate and consent the children and their families on their waiting list. The possibility of accepting an IRD donor for a prospective paediatric recipient should be discussed around the time of listing for transplantation, rather than first raising the issue around the time of organ acceptance. Patients and their families should receive careful education and counselling on the risks and benefits of implanting organs from IRD and non-IRD donors. Specific education packages and outcome prediction tools are available, but are aimed at adults, and are based on practices and data from the USA [15, 16]. Education packages should not be seen as a ‘one off’; patients should be regularly assessed as to their suitability for kidneys from IRD donors, especially those children at increased risk of poor outcomes on the waiting list (such as those running out of dialysis access, highly sensitised paediatric patients and those with rare HLA types or homozygosity).

Post-transplantation monitoring and treatment

Transplant clinicians must be aware that prospective paediatric recipients of kidneys from IRD donors should be tested post-transplant in order to detect disease transmission. Current guidance in the USA recommends HIV NAT or HIV antigen/antibody combination assay, HCV NAT, and HBV NAT and hepatitis B surface antigen (HBsAg) testing at 1 to 3 months post-transplant, with anti-hepatitis B surface antibody, anti-hepatitis B core antibody and either HBV NAT or HBsAg at 12 months post-transplant [17]. NAT testing is required as serological tests are unreliable in the early post-transplant period due to immunosuppression. We suggest that patients and their families be informed of the need for post-transplant investigations to detect disease transmission if transplantation of organs from IRD donors is considered. Transplant units should liaise closely with infectious diseases colleagues to ensure that their approaches to post-transplant testing are valid, and to facilitate early treatment of cases of disease

transmission, if they occur. Recent reports of successful eradication of HCV from recipients of known HCV-positive donors are encouraging [18, 19].

Conclusion

These data are reassuring, and the risks of BBV transmission from this donor group seem low. However, the use of kidneys from IRD donors still requires careful consideration of donor, waiting list and recipient factors. Centres must ensure that patient and family education and consent processes are appropriate, and that donor and recipient testing policies are robust. With these caveats in mind, we hope that this manuscript will stimulate the increased use of kidneys from IRD deceased donors, leading to reduced waiting times and improved outcomes for children with ESKD where there are no living donor options.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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