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Outcome of bought living non-related donor kidneys followed up at a single centre

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Abstract Between October 1985 and November 1991, 16 dialysis patients travelled to Bombay and bought kidneys from living non-related Indian donors for U. S. $ 7,372. One patient died peri-operatively; one contracted HIV and another hepatitis B virus infections. Six patients are presently positive for hepatitis C virus antibody compared to two cadaver graft recipients ($P = 0.03$); two of the six patients have chronic active hepatitis. Five-year patient and graft survival rates (75 % and 43 %, respectively) were similar to those of recipients of 24 cadaver grafts obtained in the United States (67 % and 55 %, respectively), as was graft function during the first 5 years of follow-up. Graft survival may have improved following commercial kidney transplantation in Bombay, but this practise still poses a risk of dangerous infections and exploitation of donors and recipients. The establishment of a centralized programme of anonymous "rewarded gifting" in countries that cannot eradicate rampant organ commerce may help to expunge exploitation and to ensure uniform, acceptable clinical standards and the safety of patients.

Key words Commerce, kidney transplantation · Kidney transplantation, commerce · Kidney transplantation, living non-related donor · Living non-related kidney donor

Introduction

The remarkable scope of achievements made in the field of kidney transplantation has unfortunately been limited worldwide by a shortage of donor organs, caused by the failure of physicians to turn potential donors into actual donors. Two approaches have been adopted in an attempt to redress this situation. Many countries, mostly western, are currently addressing alternative strategies to improve their rates of organ procurement [24]. However, in some poor developing countries where renal replacement services are inadequate, commercial kidney transplantation is now practised [1, 21, 25]. Even in Britain, there has been an attempt to treat kidneys like a commodity [8]. Organ commerce is unequivocally condemned by the World Health Organisation and the international and regional transplantation societies, including the Saudi National Kidney Foundation [6, 10]. In Saudi Arabia, rapid progress has been made towards self-sufficiency in cadaveric organs, thanks to the declaration in 1982 by the Senior Ulama Commission [18] that organ donation is permissible in Islam and the acceptance of the concept of brain death in 1986 by the Council of Islamic Jurisprudence [19]. An organ distribution network is now in place and an effective donor campaign has brought perceptible changes in religious attitudes. There is evidence that half of the Saudi public is willing to donate their organs after death, and over 80 % are aware of the "religious credit" to be gained by so doing [23].

Nevertheless, we have been struck by the large number of our dialysis patients privately opting to buy kidneys from abroad, frustrated by the seemingly interminable wait for cadaver grafts. Since 1985, 16 patients (32 % of our total transplants) have gone to Bombay without reference to us and bought kidneys from living, non-related commercial donors in India. We describe here their experiences and the outcome of their grafts in comparison with that of recipients of 24 conventional cadaver grafts.

Table 1 Clinical data on graft recipients grouped by donor source. LNR, Living non-related

	LNR ($n = 16$)	Cadaver ($n = 23$)	P
Age (years)	34.8 ± 13	41 ± 15	NS
Sex: Male	10	9	
Female	6	14	NS
Original disease			
Chronic glomerulonephritis	6	7	
Chronic pyelonephritis	2	6	
Henoch-Schonlein purpura	1	1	(same patient)
Hypertension	1	1	
Unknown	6	8	
Immunosuppression Regimen:			
Quadruple	0	0	
CyA + Pred + Aza	9	12	
CyA + Pred	5	7	NS
Aza + Pred	1	2	
CyA + Aza	0	0	
CyA alone	0	0	
Dosage:			
Pred (mg/kg per day)			
– at 1 month	0.58 ± 0.2	0.5 ± 0.2	
– at 2 months	0.43 ± 0.2	0.34 ± 0.15	
CyA at 3 months (mg/day)	227 ± 60	226 ± 98	NS
CyA level at 3 months (ng/ml; 95% CI)	501 (248–1000)	519 (332–811)	
Graft function (Mean serum creatinine (μmol/1)			
On return	138 ± 50	158 ± 60	
1 year	165 ± 70	170 ± 50	
2 years	187 ± 55	159 ± 64	
3 years	165 ± 80	152 ± 41	NS
4 years	148 ± 40	135 ± 31	
5 years	156 ± 49	122 ± 27	

Patients and methods

We reviewed the records of 50 patients who received 51 kidney grafts between October 1982 and November 1991. All the patients lived in Al-Baha and had attended this hospital for maintenance haemodialysis for one-half to 6 years prior to transplantation elsewhere. Forty-five patients returned to our transplant clinic for follow-up 2–6 weeks after operation. No further information was available on five patients who went elsewhere for follow-up. Sixteen patients received grafts (15 primary, 1 secondary) bought in India from living non-related donors. Twenty-three patients received 24 cadaver grafts in the United States (20 grafts) or Riyadh (4 grafts). Six patients got primary living-related grafts in Riyadh (four patients), Jeddah (one patient) or Egypt (one patient); these were excluded from the analyses. We documented age, sex, original disease, date, place and type of graft, peri-operative events, regimens and dosages of immunosuppressive drugs. All 39 patients studied had received standard immunosuppression consisting of tapering, low-dose oral prednisolone with either cyclosporin A (CyA), 5–9 mg/kg per day, subsequently adjusted to therapeutic blood levels, or azathioprine, 1.5–3 mg/kg per day, or both.

Rejection episodes were uniformly treated with 1 g methylprednisolone daily for 3 days. Four recipients of cadaver grafts in the United States additionally received monoclonal (OKT3, one patient) or polyclonal (ATG, three patients) anti-lymphocyte globulins for resistant acute rejections. Unfortunately, data on HLA typing and number of rejection episodes were not always available for comparison. CyA whole-blood trough levels were measured 3 months after transplantation using the Abbott TDx fluorescence polarization immunoassay [22]. Graft function, measured by serum creatinine level, was documented serially on the first visit and on each yearly anniversary of the graft. Our oldest grafts were done in October 1982 (cadaver) and October 1985 (living non-related). Post-transplant complications and the causes of graft or patient loss were noted. All recipients of living non-related grafts were interviewed regarding their experiences.

Data were analysed using Student's t-test. CyA blood levels required logarithmic transformation and were summarised as geometric mean and 95% confidence intervals (CI). The proportions of living non-related or cadaver graft recipients who were male or female or who were positive or negative for hepatits C antibody were compared using Fisher's exact probability test. Differences of P less than 0.05 were considered significant.

Results

Patient characteristics

There were no differences in mean age, sex, original disease, distribution of immunosuppressive regimens, doses or blood levels (CyA) of the drugs between recipients of living non-related and cadaver grafts (Table 1).

Patient and graft survival

Five-year patient survival was not significantly different between living non-related (75%) and cadaver (67%) graft recipients (Table 2).

One of 16 recipients of living non-related grafts and two of 23 patients with cadaver grafts died. The former, a 10-year-old girl who hated dialysis, died peri-operatively after a second graft in Bombay. She had a first cadaver graft in March 1990 that failed as a result of hyperacute rejection, and she subsequently exhibited persistently high titres of cytotoxic antibodies that precluded re-transplantation. In October 1991, she suddenly stopped attending her dialysis. Our further enquiry revealed that her father had taken her to Bombay where she received a living non-related donor kidney and died the following day, possibly from hyperacute rejection.

The two deaths among recipients of cadaver grafts were due to sepsis: combined pulmonary mucormycosis and candidiasis at 43 months, and cytomegalovirus (CMV) pneumonia and *Candida* septicaemia at 38 months post-transplantation.

Graft function on their return and during the first 5 years of follow-up were similar between living non-related and cadaver grafts (Table 1), and so was graft sur-

Table 2 Patient and graft survival grouped by donor source. LNR, Living non-related

	LNR	Cadaver	*P*
Patient survival (%)			
1 year	92	100	
2 years	92	95	
3 years	92	93	
4 years	89	77	
5 years	75	67	NS
Graft survival (%)			
1 year	92	87	
2 years	75	86	
3 years	67	81	
4 years	64	67	
5 years	43	55	NS

vival at 1 year (92% and 87%, respectively) and at 5 years (43% and 55%, respectively; Table 2). Four of 16 living non-related grafts and 5 of 24 cadaver grafts were lost ($P > 0.5$). Two living non-related grafts failed from recurrent focal segmental glomerulosclerosis (biopsy-proven) at 20 months and 35 months, one from chronic rejection at 14 months and one from peri-operative death of the patient (already described). The causes of cadaver graft losses were hyperacute rejection (two patients), chronic rejection at 8 months (one patient) and deaths of two patients from sepsis (already described).

Complications

One recipient of a Bombay graft was repeatedly confirmed as being HIV-positive by ELISA and Western blot; another is hepatitis B surface antigen-positive. Both had consistently tested negative before transplantation. The 31-year-old HIV-positive man, transplanted in September 1986, was only detected in October 1990 when we instituted routine post-transplant testing in response to reports of HIV transmission by living non-related kidney grafts bought in India [4]. Five years on, he is surprisingly asymptomatic, on CyA and prednisolone, and has normal renal function and lymphocyte counts.

Significantly more recipients of living non-related grafts in Bombay (six patients, including the HIV-positive patient) than cadaver grafts (two patients) tested positive for hepatitis C virus antibody ($P = 0.03$; Fisher's exact test) by the Abbott ELISA assay. None of these eight patients had been tested prior to transplantation as we commenced routine testing for hepatitis C only in February 1991. All eight patients have elevated serum amino-transferase levels; two had liver biopsies that confirmed chronic active hepatitis.

We have recently reported a staggering 45.5% prevalence of hepatitis C virus infection among haemodialysis patients in Al-Baha [3].

The frequencies of other complications (Table 3) were not different between the two groups. All four recipients of cadaver grafts who were treated with antibodies subsequently developed either CMV, herpes simplex and/or zoster infections. It is striking that 41% of our patients developed diabetes mellitus and 12.8% developed Kaposi's sarcoma following transplantation (Table 3). We [14] and Al-Suleiman et al. [5], respectively, have previously reported the relatively high incidence of these complications in Saudi patients from the Al-Baha region. Two of the five cases of Kaposi disappeared following a reduction in the CyA dose. The other three patients required additional local excision or deep X-ray therapy.

The Bombay experience

Fifteen of 16 patients got the idea of going to Bombay (and an address) from ex-dialysis patients who had been successfully transplanted there. All were self-sponsored. Initial negotiations and kidney brokerage were undertaken by their physicians in Bombay or by independent brokers who had lists of registered potential donors. The waiting time for a kidney ranged from 1 to 12 weeks (median 4 weeks). Pre-transplant work-up varied from one clinic to another. All seven clinics used by patients in this study performed blood grouping and direct crossmatch. Screening for HIV and hepatitis B apparently became consistent only after 1988.

The operations were reportedly uneventful and patients were usually discharged after 14–21 days (mean 16.4 ± 3 days). One patient developed primary graft non-function and spent 50 days in hospital. All the patients were given blood.

The average total cost of travel, hospital bed, tests, dialysis, kidney, surgery and upkeep was IR $338{,}00 \pm 71{,}500$ (Indian rupees), which approximates U.S.$ $13{,}520 \pm 2{,}860$.

The mean cost of a kidney was IR $184{,}300 \pm 85{,}000$, or approximately U.S.$ $7{,}372 \pm 3{,}400$. A few patients who met their donors later ascertained that the latter were paid only IR 36,000 – 46,000 (U.S.$ 1,440 – 1,840).

Overall, all 15 surviving patients expressed positive feelings and satisfaction about their experiences in Bombay. Each has since given an address to at least one other dialysis patient. On their return, they brought discharge letters of varying detail, but all were conversant with the dosages of their medicines. All 15 patients had stable renal function on arrival, but 2 required immediate admission, one for herpes zoster and acute epididymo-orchitis, the other for acute cholecystitis.

Table 3 Post-transplant complications grouped according to donor source. LNR, Living non-related

	LNR ($n = 16$)	Cadaver ($n = 23$) (24 transplants)
Infections		
HIV	1	0
Hepatitis B	1	0
Hepatitis C	6	2 ($P = 0.03$, Fisher)
Herpes simplex + zoster	2	5
Tuberculosis – miliary	2	0
– pulmonary	0	1
Pneumonia – bacterial	2	6
– fungal	0	2 (both fatal)
– CMV	1	1
Septicaemia – bacterial	0	3
– candida	0	1
– CMV	0	2
Gastroenteritis	1	3
Urinary tract infection	2	1
Renal transplant abscess	1	0
Epididymo-orchitis	2	0
Otitis media *(Pseudomonas)*	0	1
Cellulitis	0	1
Cholecystitis/empyema	1	2
Other complications		
Diabetes mellitus	8	8
Kaposi's sarcoma	1	4
Hypertension	8	14
Hirsutes	1	4
Hyperlipidaemia	3	7
Polycythaemia	1	1
Transplant obstruction	1	0
Steroid cataract	0	1
Renal tubular acidosis	1	0
Gingival hypertrophy	0	1
Myocardial infarction	0	1
Transient ischaemic attacks	1	0
Aseptic hip necrosis	0	1
Infertility	1	0
Intrauterine foetal death	0	2 (same patient)
Successful pregnancy	0	1

Discussion

Results from this study confirm the high risk of infection with dangerous viruses previously reported among recipients of kidneys bought from living non-related donors in India [1, 4, 21]. Salahudeen and his colleagues [21] described 130 such patients from the United Arab Emirates and Oman, 24 of whom died early in the first year (81.5% survival) mostly from infections, including the acquired immune deficiency syndrome (AIDS) and acute hepatitis B. Abouna and co-workers [1] reported a similar experience among 110 patients from Kuwait. Our two patients infected with HIV and hepatitis B were transplanted in 1986 and 1988, respectively, before routine screening was instituted at many centres used by the patients in this study.

AIDS usually develops 1.5–2 years following infection in immunosuppressed transplant recipients, as compared with 7–8 years in normal hosts [20]. That our HIV-positive patient remains asymptomatic 5 years on raises the possibility that he may have acquired the infection more recently, although he denies indulgence in known risk practises. Regrettably, none of the seven Bombay clinics seemed to have tested for hepatitis C, which can also be transmitted by organ transplantation [16]. It is likely that some of our six positive patients were infected by their grafts from Bombay. In this series of patients, in contrast to those reported in the foregoing studies [1, 4, 21], 5-year patient and graft survival and graft function were similar to those of our patients who received cadaver grafts in the United States, and they compare favourably with results of cadaveric kidney transplantation in Europe [9]. One reason for this apparent difference in outcome may be that our study population was relatively small and may have lacked the power to detect subtle differences. However, it is probable that most of our patients selected the better units in Bombay, having been informed by others who had been successfully transplanted. This suggestion is strengthened by the finding that our patients paid a lot more for their kidneys (U.S.$ 7,372 on average) than did those studied by Salahudeen and his co-workers (U.S.$ 2,950) [21]. Alternatively, our better results may reflect the fact that our study extended almost 4 years longer – a period over which the Bombay teams may have improved their surgical techniques and strategies of peri-operative care and immunosuppression. The good survival figures from this study support the conclusion by Al-Khader and colleagues [2] that poor results should no longer be cited as part of the argument against commercial kidney transplantation, because the results have improved. However, the risks of operative mortality and hepatitis or HIV infection remain unacceptably high.

Living non-related kidney donation is ethically acceptable only when the organ is not purchased [10], such as in emotionally related or the rare altruistic donation. "Rewarded gifting" [21] – living non-related donation with a compensatory incentive – is slowly winning support among prominent members of the profession in North America [7, 11, 12]. Its advocacy centres around the argument that "kidney donation is a good act. It is a gift of life. The financial incentive to promote such an act is moral and justified" [15, 17].

Rampant commercialism – exemplified by the patients described in this paper – is morally, ethically and medically unacceptable. This and other studies [1, 4, 21] have clearly shown that it exposes patients to a high risk of death and serious infections, relaxes normal standards of transplantation practise and leads to exploitation of donor and recipient. It may also deter the much-needed development of cadaver donor programmes in emergent nations.

Sadly, commercial transplantation continues to thrive in some developing countries, in spite of our justified and

staunch opposition to it. Patients who consider themselves helplessly condemned to a lifetime of dialysis embrace this tantalizing option as their only hope to buy the "gift of life" and be liberated from dialysis. What is to be done about commercial kidney transplantation? What role should we, as renal physicians, play in the developing world? Our elite attempts to dissuade patients on the basis of sound ethical, moral and medical arguments fail. They fail because the difference is clear to everyone following each successful trip to Bombay. We have no magical equivalent to offer those who we ask not to go, except a cheerless, forlorn hope for a cadaver graft that may not materialise.

Should we legislate and prohibit it, ignore it, or should we strive to reform commercial kidney transplantation?

Legislation will surely drive the practise underground to the further detriment of patients and may seem in the Third World like denying these patients the right to live. To ignore the practise would be to tacitly permit its continuation in the present form, with all its inadequacies and dangers to patients and society. Our experience with this problem has led us to believe that paid kidney donation is inevitable – albeit unethical – in emergent nations where there is poverty and where renal substitution services are under-developed. Patients will continue to buy kidneys, against our expressed wish. One realistic approach to this problem may be to advocate central control in order to purge this practise in those countries where it cannot be effectively prohibited. The medical authorities in such countries could establish national programmes to centralize the donor pool, remove exploitation, and ensure adequate pre-transplant work-up, screening for infections, uniform acceptable clinical standards, fair donor compensation and proper follow-up.

By so doing, perhaps the present rampant commercialism could conceivably be transformed into a system of anonymous "rewarded gifting" sanctioned and supervised by government. Potential donors might even be matched with recipients as in present-day conventional programmes. As Monaco suggested [13], "under such a system, the recipient would not buy an organ from some donor, nor would the donor sell an organ to the recipient. Rather, the government would provide a direct subsidy to the donor after the transplant has been performed."

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