Cadaveric renal transplantation in the Kingdom of Saudi Arabia

Abdullah A. Al-Khader

Department of Nephrology, Riyadh Armed Forces Hospital, Riyadh, Saudi Arabia

The development of renal transplantation in Saudi Arabia

Background

The first renal transplant operation to be carried out in the Kingdom took place in March 1979—a daughter to father donation. It was clear even then that end-stage renal failure (ESRF) was quite common in the country. Reports since then estimated it to be over 100 per million per year and in the south, where malaria and schistosomiasis are prevalent, the incidence is even higher. The Kingdom of Saudi Arabia is a vast country with an area of 2.5 million sq. km and a population of 17 million according to the 1992 census. It contains the two most sacred Mosques for Moslems all over the world, in Mecca and Medina which every able Moslem is obligated to visit at least once in his/her lifetime.

Facilities

Initially, only live related transplantation was undertaken in Riyadh Armed Forces Hospital (RAFH). Concomittant with this, Saudi doctors were undertaking training in renal (and indeed organ) transplantation in USA, Canada, UK and Germany and eventually came to run their own renal transplant programmes in various hospitals in the Kingdom. Currently, there are 11 such centres in all the five regions of the Kingdom (north, south, west, east and central). All are run by local teams. In addition, there are three liver transplant centres, two heart transplant centres and eight cornea transplant centres.

Life donor transplantation

As mentioned above, all early transplants were from live related transplantation. (The only two exceptions being spousal donations and donations from breast milk kinships—as outlined and governed by Islamic ruling in this connection.)

Because of the large families we have and the importance of supporting kinship that Islam directs there have been many willing donors. However, it is of interest that the majority of donations come from siblings or offspring and relatively small numbers of donors are parental, unlike the case in the West [1]. Nevertheless, it was clear from very early on that live donation was not sufficient by any stretch of the imagination, as indeed, is the case universally.

An Intermezzo—out of Country transplantation

We were determined (and still are) not to allow commercial transplantation for the well debated ethical reasons and knowing that it will kill off our live related programmes and impede the cadaveric programme.

As a result, many of our patients had to go abroad for transplantation and we received patients from many countries but the majority were from USA and India. Transplantation in USA proved costly (an average 200,000 dollars for each transplantation) and transplantation in India had its own ethical and medical problems [2,3].

The answer to these problems was, of course, to establish a local cadaveric programme.

Approval of religious authorities

The Saudi Arabians are deeply religious people; virtually in every action they take, they are guided by the teaching and guidance of Islam. It was therefore necessary before starting a transplantation programme to seek the opinion and approval of our religion through discussions with religious leaders.

A series of meetings took place regarding live related organ donations, cadaveric organ donations, brain death and cessation of therapy in brain death patients all from the Islamic view point. All these concepts were found permissible from Islamic point of view under strict adherence to proper and accurate diagnosis and application of the highest standard of medical practice and ethics. Commercial transplantation was, however, found unpermissible.

The Eurotransplant experience

Before establishing our own cadaveric programme we went through a very useful step in the development of
renal transplantation. This was through obtaining cadaveric kidneys donated from Eurotransplant. Between 1983 and 1988, about 55 such kidneys were generously donated free of charge. Very often these kidneys were rejected by European centres or when suitable recipients were not found. Significant number of them were suboptimal (old donors, donors with controlled hypertension, half a horseshoe kidney and even a kidney which has been previously transplanted [4] as well as kidneys in acute tubular necrosis).

In virtually all the patients there was a long cold ischaemic time (mean 42 h range 24–72 h) and the vast majority had long primary non-function [5]. Again, as in other phases of our renal transplant programme we have learnt a great deal from this phase. We learnt about the logistics of shipping organs over long distances and about suboptimal kidneys. It encouraged us to be ‘bold’ in accepting kidneys which hitherto been considered unsuitable. We also learnt that it is possible to use cyclosporin even with primary non-function and long ischaemic time with good short [5] and medium-term patient and graft survival [6].

The donor and recipient pool

Unfortunately, the potential number of brain dead cases in the Kingdom is enormous and will cover the needs for all organ transplantation due to high incidence of road traffic accidents. It is estimated that road traffic accidents lead to 3000 deaths per year. Most concern young individuals. Our Intensive Care Units (ICU) are full of road traffic accident victims. There are 110 ICUs, in all areas in the Kingdom.

The waiting list for kidney transplantation is estimated to be 2500. On the other hand the number transplanted in 1997 was 267 kidneys (15.7 pmp).

The early steps of a cadaver transplant programme

After obtaining religious permission for cadaveric donation, the stage was set to start the programme especially after technical and logistic considerations had been sorted out.

The first opportunity occurred in December 1984, when the family of a Saudi child involved in fire tragedy agreed to donate the child’s kidneys and the first two cadaveric transplant operations were carried out at the Riyadh Armed Forces Hospital [7]. This event broke the psychological barrier, since prior to that event we had underestimated the Saudi citizen’s willingness to donate and we had approached the first family with great trepidation and even fear. Later on, a number of studies aimed at exploring attitudes for donation were undertaken [8,9] and showed that a large proportion of the population have a positive attitude towards donation. This is related to the fact that religious approval has been obtained for this act.

The organizational and logistic infrastructure

It became rapidly apparent that a national body to regulate, encourage and adopt organ transplantation had to be established. This culminated in the establishment of the National Kidney Foundation by a Royal order in 1985. It has since been supported fully by the government which realized the major problem of organ failure and the need to do something about it.

This foundation had many functions including overseeing regulations governing organ transplants, encouraging donations, education of medical personnel and public, supporting the medical services, updating waiting lists, liaising with ICUs and transplant centres, overseeing coordinators, doing research and running the only journal in the Arab world on kidney diseases (The Saudi Journal for Kidney Diseases and Transplantation). Many committees were formed including prominent medical, religious and social personalities to address all the above aspects. The centre is linked through computer terminals to 40 major dialysis units. The centre sponsors regular open days for school children as well as public and media campaigns.

This effort culminated in what will probably become the most successful cadaveric organ transplant programme in the Islamic world [10,11].

Due to the clear need for multiorgan donation, the National Kidney Foundation was changed, by Royal order, to become the Saudi Centre for Organ Transplantation (SCOT) in 1993, and its function was expanded to cater for all organs.

As mentioned earlier, the Kingdom is a vast country and we are helped by the medical air evacuation system of the Ministry of Defence which was put at the disposal of SCOT. So far, 300 flights were performed by this facility in support of organ donation—inside and outside the country.

To help improve the number of donations a system was set up by SCOT in 1994 by which each transplant centre became a nucleus for support to a number of hospitals ICUs, and dialysis centres (there are 110 dialysis centres) for the purpose of mutual support, organ harvesting, provision of experts in organ failure, brain death diagnosis and maintenance of organs. This system has made a big difference and resulted in a significant rise in the number of organs donated.

The next step that SCOT undertook was coordination with the Arabian Gulf countries under the auspices of the Gulf countries council (GCC). To that end, an inter country permanent committee was set up for organ transplantation. This meets regularly. Already, exchanges of organs have taken place between these countries (Saudi Arabia, Oman, United Arab Emirates, Qatar, Bahrain and Kuwait) and the first GCC Conference on organ transplantation took place in Abu Dhabi in February 1998.

Workers in the field of transplantation in Saudi Arabia have made interesting observations in this field which have been presented in international meetings and published in international journals.

It may be of interest to highlight some of these findings that are of particular relevance for the Middle East Region.
The Saudi experience with cadaveric organ transplantation

Organ retrieval

Until 1993, only kidneys were harvested. From 1994 onwards other organs were harvested as well. So far, the number of cadaveric organs transplanted are 910 kidneys, 148 livers, four pancreases, 74 hearts, 134 heart valves and five single lungs.

We have found that 45% of potential donors were rejected for medical reasons. Of those 69% were due to multiorgan failure and 13% were due to sudden cardiac arrest and 6% were due to systemic infection [12].

This was clearly the result of delays in reporting, diagnosis of brain death and inadequate maintenance of donors. We started an intensive campaign to educate medical and nursing personnel involved in ICUs [11] (there are 110 ICU units with 1005 ICU beds in the Kingdom). So far, 1230 ICU doctors and 960 ICU nurses have attended our courses. As a result, we are seeing a reduction in the rejection of organs due to medical reasons [13]. Of the kidneys harvested only 5% were not used and about half of these were due to anatomical anomalies [14].

Family consent

Overall, we were able to obtain consent in 34% of documented brain death cases. This rate of consent has not improved over the years, unfortunately [15]. It should be noted that we require the consent of the families before harvesting can take place. We found that consent is more likely to be forthcoming if the potential donor is male than if it is female and is more likely in younger donors (0–20 years) than in older donors (21–40 years) [17].

Unfortunately, as mentioned earlier, road traffic accidents are quite common in Saudi Arabia, and those involved are young adults. We found that the mean age of brain dead donors was 23.6 ± 14.1 years and the cause was road traffic accidents in 61% of the cases followed by cerebrovascular accidents in 13% and anoxic brain damage in 8% of the cases [16].

Patient and graft survival

Single unit observations of patient and graft survival are comparable to leading units in the world (over 96% and 90%, respectively, after 1 year) for live related transplant [18,19]. For cadaveric transplantation the results are also excellent (over 95% and 78%, respectively) [18,19].

So far, 2500 live related transplants and 910 cadaveric transplants were carried out in the Kingdom.

Paediatric age groups

Among the Kingdom’s population, 53% are below the age of 18 years. Reports appearing so far suggest that the incidence of ESRD in Saudi children (7.3% per million per year) is higher than that in the West. Moreover, congenital and hereditary causes are the predominant aetiology in the children [20]. This may be due to the high incidence of marriages within families (53%). Preventive measures such as pre- and perinatal ultrasound examinations are carried out routinely and today such abnormalities are corrected. This hopefully will lead to reduction of incidence of ESRD.

Malignancy

By far the commonest malignancy encountered is Kaposi Sarcoma [21–23]. It accounts for 85% of all post-transplant malignancies and is estimated to occur in 4.7% of all transplant patients [22]. The majority of patients develop this malignancy within the first year of transplantation and interestingly it is commoner in the patients from the Southern region of the Kingdom in whom it occurs in 7.4% of the patients especially in males (11.7%). It has a worse prognosis when it involves the lungs [22] and when it occurs in children [24]. Otherwise, in the majority it regresses by either reduction or cessation of the immunosuppressive therapy [21,22]. It should be noted that this tumour is rare in the general population of Saudi Arabia (0.1% of all malignancies).

We found that the risk of Kaposi Sarcoma is greater with cyclosporin than with azathioprine [25] and that the tumour recurs following the reintroduction of immunosuppression [25].

We have also seen a number of cases of lymphoma, but this tumour is rare compared to the western experience, although the tumour is relatively common in the general population of Saudi Arabia [26].

Tuberculosis

The incidence of tuberculosis is 0.5% in the general population of Saudi Arabia [27]. The incidence is 4.6% in transplanted patients [27,28]. In the majority of cases, provided that there is a high index of suspicion for tuberculosis, the patients do well with standard anti-tuberculosis therapy. Interestingly, renal tuberculosis has to be considered in the differential diagnosis of deteriorating transplant function associated with fever. In these cases, the diagnosis can only be made by graft biopsy which reveals tuberculous interstitial nephritis. Virtually all such cases end up with graft loss [27].

Rifampicin reduces cyclosporin levels. We found that one can use cyclosporin and rifampicin simultaneously and obtain the desired cyclosporin level by quadrupling the maintenance dose and giving it in three divided doses [29].

Viral hepatitis B and C

The prevalence of hepatitis B in the Kingdom is 8% with regional variations [30], but is expected to fall in the future after adoption of a universal vaccination policy at birth. A study of hepatitis B in our transplanted patients showed that the renal and hepatic
prognosis is good, provided that a pre-transplant liver biopsy showed no or minimal abnormality. This is true even in the presence of E antigen; in contrast the presence of delta antigen, universally leads to severe liver disease [30]. Again, due to the high prevalence of this virus in the population we used HSAg positive kidney donors with no problems, provided the recipient is immune. Nevertheless we give a booster vaccination and hyperimmunoglobulin at the time of the operation [31].

The prevalence of hepatitis C is only 1.5% in the general population but it is high in our dialysis population [32]. Isolation policies have reduced this prevalence. We are not yet sure whether transplanting hepatitis C positive patients worsens the hepatic prognosis; but we have a policy of biopsying their livers pre-transplantation and transplant only patients with near normal findings. Among our transplanted patients almost 54% carry the virus and our observations showed that 28% of these patients have biochemical and/or liver biopsy evidence of chronic liver disease after a mean follow-up period of 53 months.

**Pregnancy post-transplantation**

As part of our culture, we tend to have large families. As such, the prevalence of pregnancy post-transplantation is almost 50% in women capable of child bearing in the post-transplant population compared to only 3% in the West [33].

In our institution alone, there were 54 such pregnancies in 35 women. Our findings would suggest that with good renal function and easy to control BP, it would be safe from the mother's and baby's point of view for pregnancy to take place [34]. There is, however, an increased incidence of rise in BP, gestational diabetes mellitus and requirement to increase cyclosporin dose in the second trimester [33]. There is also an increased incidence of caesarian section and small for date babies. We have reported 17 successful pregnancies in three women [34], and found normal renal function in 22 such babies (whose mother received cyclosporin during pregnancy) after a follow up period of 43 months [35].

**Fasting Ramadan**

Moslems fast 1 month (Ramadan) every year from sunrise to sunset (with abstinence from foods and fluids). This is a religious obligation for all except those who have an illness which could be adversely affected by fasting.

Our findings strongly suggest that after 6 months of successful transplantation (near normal renal function) the kidney hypertrophies normally [36] and can cope with fasting by maintaining renal function and is capable of concentrating the urine adequately [37].

**References**