

## Ethical issues in organ transplantation

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Pakistan's image as civilized society has been tarnished in recent years because of several factors. One of the factor had been human organ ("Kidneys") trade which has shifted from India to Pakistan. Media, in particular had gone to the extent of labeling it as shifting of "Kidney Bazar", "Bombay Bazar" from India to Lahore and Islamabad.

We as a nation have failed to promulgate cadaveric law. Even the medical community is not aware of the curse of non-related renal Transplantation

in Pakistan. You discuss the dilemma of Kidney trade even with medical students and young doctors, they may have opposite opinion and perceive it as a "life saving" procedure. They may not be able to differentiate between "Altruistic" and "Commercial interests" involved in the "trade" of renal transplantation. This review will highlight some of the ethical aspects of this important topic concerning our nation at this time of actual implementation of Cadaveric Law.

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Organ transplantation is the primary technique for the treatment of end stage organ failure and has benefited more than one million persons worldwide. A number of patients have survived for well over 25 years and survival rates at 5 years can be 70% or higher for many organ transplant programs. However, currently more than 40,000 patients are waiting for a kidney and in Western Europe mortality rates for patients waiting for a heart, liver or lung range from 15 to 30%. The potential need for transplants is even greater and this imbalance between supply and demand creates technical and ethical problems including the risk of organ trafficking. Consequently the number of available organs must be increased. In some cases the organ shortage reflects a true lack of donors, but more often it results from the failure to turn potential into actual donors. The transplant commission of the Council of Europe has just approved a document recommending that member states ensure that all potential donors are identified and as many as possible be converted into actual donors. Even with the highest organ donation rate, the indications for organ and tissue transplantation will continue to increase, perpetuating the gap between supply and demand. Organ transplantation, whether living or cadaveric, might be supplemented or replaced by the use of artificial organs, although problems such as thrombosis, infection and biocompatibility pose

obstacles to long-term function. The use of animals as an alternative source is considered, but so many problems still remain unresolved that xenotransplantation could not be put forth as a solution to this problem [1].

Transplantation constitutes a rapidly changing field for medico-legal law- makers. Until two or three decades ago there were no laws governing organ transplants and at least some of these processes fell within the realm of human experimentation. An extensive legislative work has been accomplished since then in order to catch up with the expeditious scientific progress. Transplantation is a definite medical process that requires a definite legal response. No wonder that some issues are dealt with by national laws in similar manners. Nevertheless, practice makes perfect and recent legislative have gained experience and drawn their lessons from the former ones. There are many issues like distribution of organs, costs and donations, the removal when and how allowed and restrictions and conditions of removal which need discussion. These and other issues have recently been formed by the following legislatures: Argentine, Canada, Columbia, Finland, France, India, Italy, Krygystan, Mexico, Peru, Portugal, Romania, Russia, USA and by the Council of Europe [2].

Ethical issues have always been apparent in the transplantation process and are becoming more

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evident as the demand for the organs increases. The basic question is how just and ethical are the new policies enacted to encourage organ donation, considering that they effect the total public and benefit the small percentage of patients who require transplantation [3].

### **LIVING ORGAN DONATION**

Living organ donation can be either related or non-related. Related where a first or second-degree relative donates and non-related where any body else donates. Living organ donation is unique in the field of surgery that the operation is performed on a subject for not its benefit and rather has physical disadvantages. That is why living organ donation is not a favoured option in the developed countries. It constitutes only 3% and 10% of the total renal transplantation in France and U.K. respectively [4]. Therefore, before embarking upon living organ donation, it needs full justification. Renal transplantation is the most common and acceptable form of living organ donation all over the world and therefore, most of the discussion and debate revolve around it.

**Living Related Organ Donation:** It is presumed to be the most ethical form of organ donation. One can argue that the psychological and non-specific benefits to the donor are real, particularly when a close relative is returned to normal health. There can, however, be no doubt that the physical consequences of living donation are entirely detrimental to the donor. Motives behind the 1st degree living renal donation are understandable and one may assume that the living donation between relatives carries the same altruistic motives. In related organ donation, the donor saves the life and attains the well being of its immediate relative by accepting a physical injury and debilitation to itself. While many related donors fall neatly into this altruistic categorization, unfortunately, there are many examples where the related donors have attained physical, emotional or financial toll from the recipient.

From the recipient point of view, there are two specific advantages, which may be conferred by living related donation. The first is that transplantation can be planned to the recipient's need under best possible circumstances and second comes from the improved results of renal transplantation from living related donors [5].

**Living Non-Related Organ Donation:** The rationale for non-related and unmatched donation is much harder to define in the same scientific terms as for matched related donation. There is certainly no clear advantage to unrelated donation in terms of graft or patient survival when one compares unmatched living with cadaveric donation. There is, however, a difference in the initial function rate, with living donors not surprisingly providing the most reliable initial function [6].

There are number of different issues that have to be analyzed when the living donor is unrelated to the recipient. The various situations can be:

- **Altruistic Organ Donation:** One must consider the unrelated donor who has a stable and close emotional relationship with the recipient, such as a husband or wife. A shortage of cadaver donor organs requires transplant units to examine all possible alternatives. Transplantation from living donors accounts for only approximately 10% of kidney transplants in U.K. Recent studies have shown that the results of kidney transplantation between spouses are at least as good as those of well-matched cadaver organs, but very few transplants of this type have been performed in U.K. so far. As part of the assessment process, the proposed donor and recipient are required to provide written statements about the issues. It is believed that the statements support the contention that spousal transplantation is ethically justifiable and should be more widely available[7]. Stimulated by a severe organ shortage and an improving ability to successfully transplant poorly matched donor-recipient pairs, many transplant centers are now willing to accept emotionally related (but genetically unrelated) people (e.g., spouses) as kidney donors. To see whether this practice is encouraged, a survey was mailed to all 209 adult renal transplant centers in the United States. Of the 154 (74%) responding centers, 90% said they accept emotionally related donors and 60% said they actually encourage this practice. Nearly 40% prefer spouses to cadavers, while only 21% prefers friends to cadavers. To further explore the degree to which emotionally related donation is encouraged, a second questionnaire was sent to a sample of centers (n=51) that support this practice; 94% responded. While only 44% said they encourage the use of friends, nearly all of these pre-selected centers said they encourage spouses to donate. On the other hand, judging from their stated approach to this

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issue, only about half of these supportive centers seem to actively encourage emotionally related donation. These data suggest that, overall, at most only about one third of U.S. transplant centers actively encourage spousal donation and at most about one quarter encourage the use of friends. Consistent with these results, emotionally related donors contribute only a small fraction of all kidneys transplanted in U.K. If the large potential contribution of emotionally related donors is ever to be realized, transplant centers must go beyond simply accepting such individuals and begin to actively encourage their participation. Medical and ethical considerations strongly support this proposal [8].

- **Paid Organ Donation:** It is an important ethical issue in organ transplantation. Whatever the perceptions of this practice in developed countries, it is widespread across the world. There are regional variations in its acceptance and practice. In France it is crime to get involved in paid organ donation [4]. Most of the international organizations and forums have called for a moratorium against the sale of organs [9, 10, 11] but the debate is not yet over.

Recently the existing arguments against paid organ donation have been re-examined and found to be unconvincing. It is argued that the real reason why organ sale is generally thought to be wrong is that (a) bodily integrity is highly valued and (b) the removal of healthy organs constitutes a violation of this integrity. Both sale and (free) donation involve a violation of bodily integrity. In case of free donation the violation of bodily integrity is typically outweighed by the presence of other goods: mainly, the extreme altruism involved in free donation. There is usually no such outweighing feature in the case of paid donation. Given this, the idea that we value bodily integrity can help to account for the perceived moral difference between sale and free donation [12].

Recently, Cameron and Hoffenberg from U.K. have examined the arguments for and against the practice of paid organ donation and the use of judicially executed prisoners as seen in the world context. Although Western opinion is almost universally against both practices, they seek to establish that this has arisen largely from justification of an initial revulsion against both and not from reasoned ethical debate. In examining the most commonly cited arguments against these practices;

they demonstrate that this revulsion arises mainly from the abuses to which both processes have been subjected, rather than the acts themselves, together with opposition to a death penalty. At the moment and for some future time, in the absence or shortage of dialysis in large parts of the developing world, transplanted organs represent the only means of treating end stage renal failure. Thus, a clear ethical conflict arises as to whether greater harm or good is done by allowing individuals to die or adopting strategies for obtaining organs that raise ethical problems. They call for continued reasoned ethical debate on both issues, rather than accepting that the argument is already over [13].

It is time to re-consider the pool of living donors without encouraging the commercialism. The different suggestions [14] put forth are:

- Encouraging donations by genetic relatives.
- Allowing volunteers a greater voice in determining their own suitability.
- Encouraging the use of emotionally related individuals and accepting altruistic strangers.
- Considering motivated identical twin minors and older adolescents as donors.

## **MINORS AS DONORS**

It is another issue that needs considerate discussion. Living donors provide the best outcome for children undergoing renal transplantation. Most of these donors are parents. When parents are unable to donate, siblings are often considered. But what if the siblings are also children? Should they be permitted to donate?

Most U.S. transplant centers are opposed to using children as living kidney donors. On the other hand, a careful analysis of this issue suggests that although donation by a minor should be uncommon, a complete ban of this practice may be unwarranted. In unusual circumstances in which no other suitable donor is available, consenting mature minors and even rare immature minors who are highly likely to benefit from donating, may be ethically acceptable. Although there are probably no absolute wrong or right answers, the question of kidney donation by children should be readdressed [15].

Over the last few decades there has been a substantially higher percentage of successful organ transplants but also a significant imbalance between the demand for and the supply of organs, creating the basis for a highly profitable black market trade in

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human organs. Sometimes there are reports that children have been kidnapped, only to reappear later lacking one kidney, or that they simply disappear and are subsequently killed to have all their transplantable organs removed for profit. The European Union feels that there is a need for action and that it has a duty to act in this field, especially for ethical reasons. There is now established close co-operation between the various European transplant organizations. The legal protection of children with regard to organ transplantation is not specifically mentioned in the existing conventions because this issue was not foreseen at the time of their preparation. However, the issue is covered in a broader sense by more general provisions. There are endless rumours surrounding this area. Members of various organizations who travel in the suspected countries say that the trafficking in children who are sold for transplantation is well known, but it is too difficult and very dangerous to catch the people involved [16].

#### **CADAVERIC TRANSPLANTATION**

Organs for transplantation are usually obtained from living genetic relatives or from heart-beating cadavers. Unfortunately, these sources have so far been unable to keep up with demand. As a result, there are a large and steadily increasing number of potential recipients awaiting transplantation, some of whom will die before an organ can be found. This scarcity of organs for transplantation can only be met from the cadavers. Cadaveric source is beneficial in another way that it provides multi-organ donation [17]. To utilize cadaveric organs effectively, it needs legal formalities and most of the countries have passed cadaveric law [2, 18]. In an attempt to rectify this tragic situation, several suggestions have been proposed for increasing the pool of cadaveric donors [14]. These include:

- Overcoming the family consent barrier by presuming consent, mandating completion of binding advanced directives or by eliminating the need for consent entirely.
- Reconsidering non-heart beating donors.
- Elective motivation for organ donation.
- Accepting organs from anencephalic infants before brain death occurs.

All of these proposals raise concerns. Those approaches considered to be ethically acceptable and to hold promise for success should be vigorously pursued; beginning with carefully designed pilot studies. Hopefully, such an approach will eventually

increase the number of organs available for patients suffering from end-stage organ disease.

#### **XENOTRANSPLANTATION**

The success of all transplantation as a treatment for end stage organ failure has resulted in the need for an increasing number of organ donors. Attempts to meet this need include the use of organs from living related and unrelated donors, financial or other incentives for the donor family and even the reuse of transplanted organs. Despite these initiatives, the supply of organs for transplantation still falls far short of the demand, as evidenced by longer waiting times for transplantation and decreasing transplantation rates. Even if Canada were able to increase its organ donor rate to that of Spain (40 to 50/million), where organ donation is governed by “presumed consent” legislation, this would not alleviate the problem of donor shortage. Severe shortage of human organs has created interest in xenotransplantation. Indeed, some argue that xenotransplantation is the only potential way of addressing this shortage. As immunological barriers to xenotransplantation are better understood, those hurdles are being addressed through genetic engineering of donor animals and the development of new drugs therapies [19].

The focus of ethical attention has changed from the moral correctness of using animals for research/therapy to an increasingly appreciated danger of the establishment and spread of xenozoonoses in recipients, their contacts and the general public. The United Kingdom has established an embargo on clinical trials and has set up a national regulatory authority to oversee and coordinate the development of research, establish guidelines and decide on when trials can proceed. In the United States, on the other hand, the overall attitude is to “proceed with caution” and the Food and Drug Administration has approved a number of xenotransplant studies. The Public Health Service guidelines on reducing infection risk are still evolving and are likely to end up being more cautious than they are currently. There are a number of reasons for not using subhuman primates for xenotransplantation, including their closeness to humans, the likelihood of passing on infections, their availability (gorillas, chimpanzees), their slow breeding and the expense of breeding them under specified pathogen free conditions. The pig, although domesticated and familiar, is too distant to evoke the

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same feeling as we have for primates, has the correct-size organs, is probably less likely to pass infections, breeds rapidly and is not endangered; moreover, millions of them are eaten every year. Although drawing ethical conclusions is difficult at the stage of knowledge and debate, it seems acceptable to manipulate pigs genetically and to proceed to using their organs for xenotransplantation trials when infection control measures and the scientific base justify it. The use of pigs in Muslim countries would be more controversial and disruptive. In this case the question of informed consent is likely to be ambiguous and awkward. It might end up more of a binding legal contract than consent, as we understand it now. Xenotransplantation is also unlikely to cost less than or significantly alleviate the shortage of, cadaveric organs in the short term. The international dimension of the risk of infection is becoming obvious, but there has so far been no effort to convene an international forum to agree on universally acceptable guidelines [20].

However, before xenotransplantation can be fully implemented, both the scientific/medical communities and the general public must seriously consider and attempt to resolve many complex ethical, social and economic issues that it presents [21].

### **THE FUTURE!**

The future of organ donation depends on how to correct the scarcity of organs for transplantation. Is it to pass the cadaveric law, applicability of xenotransplantation or recently to apply the art of cloning for the shortage of organs?

The first two possibilities have already been discussed in detail. The most publicly justifiable application of human cloning, if there is one at all, is to provide self-compatible cells or tissues for medical use, especially transplantation. Some have argued that this raises no new ethical issues above those raised by any form of embryo experimentation. It is argued that this research is less morally problematic than other embryo research. Indeed, it is not merely morally permissible but morally required that we employ cloning to produce embryos or fetuses for the sake of providing cells, tissues or even organs for therapy, followed by abortion of the embryo or fetus [22].

Although the conscience and character of a good doctor are sufficient on their own to allow us to discuss and make decisions regarding very difficult ethical subjects in transplantation, basic ethical principles commonly used in medicine must also be

applied to various aspects of organ donation. Some system has to be adopted that assesses the weight that must be given to various possible solutions. For example, would live donor transplantation still be acceptable if there were an excess of cadaveric organs? If animal organs can be transplanted successfully, is that more desirable than using human organs: particularly if human donation involves interventional ventilation or non-heart beating donors? Is interventional ventilation more ethical than live donor liver or lung transplantation? No doubt future developments in transplantation, opening more opportunities for the successful treatment of more patients, are likely to produce increasingly difficult ethical issues. Discussions of these issues must be firmly based on principles of medical ethics, although accepting that whilst absolute principles may be available, absolute answers are more difficult to come by [23].

Sale and purchase of kidneys is rampant in Pakistan. Recently an ordinance "Removal, Storage and Transplantation of Human Organs and Tissues for Therapeutic Purposes" has been promulgated by the President of Pakistan. Hopefully it will put an end to the blatant commercialization of organ transplantation and the unscrupulous kidney trade.

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