Global Education Initiatives

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Organ transplantation has progressively become the best, and sometimes the unique therapeutic alternative for patients with end-stage organ failure and many other life-limiting conditions. Thanks to the continuous improvement in immunosuppressive therapies and surgical techniques, transplantation today does no longer represent an experimental procedure, but a well-established clinical therapy, which saves the life or enhances the quality of life of thousands of patients every year. According to estimations from The Global Observatory of Donation and Transplantation (1), there are almost 100,000 solid organ transplants performed annually all around the world.

The impressive evolution of organ transplantation activity in a 50-year period is greatly related to the extraordinary results obtained with this therapy, which have been progressively improving for the different types of solid organ transplants (2–4). These results are well represented by the longest survivals described by Cecka and Terasaki (5) for transplanted patients: up to 45, 38 and 29 years for a kidney, a liver, or a heart transplant recipient. However, these excellent results have led transplantation to become a victim of its own success. Organ shortage is a universal problem that precludes transplantation from developing to its maximum potential and that is related to a wide set of individual and global consequences.

THE FIGURES OF ORGAN SHORTAGE

Difficulty of getting accurate and transparent figures in transplantation activity is highly increased when we get to the point of analyzing the needs. There is no global and accurate estimate on the number of patients in the waiting list for a transplant, but a simple exercise can be performed by calculating the number of patients in the list in the event the same criteria applied in Spain (6) were extrapolated to the world population. The result would be no less than 1 million people potentially getting a benefit from organ transplantation each year: 10-fold the estimated number of transplanted patients (1).

However, it is clear that any approach to the number of patients in the waiting list is always an underestimation of the needs. Focusing on the kidney, end-stage renal disease (ESRD) has become a universal health problem, with more than one million and a half patients on dialysis therapy (Luc Noel, personal communication) and 66,000 kidney transplants performed each year (1) (Fig. 1). However, there are marked differences in the number of patients per million population accepted for renal replacement therapy in the different parts of the world (7). These differences might be partially explained by epidemiological aspects (as it is the case of Japan) but mainly by economical reasons.

Hence, demand is well over the supply of organs for transplantation, according to current figures that possibly underestimate the real needs. Finally, demand is expected to be increasing in the near future, particularly when referring to kidney transplantation. It has been estimated that the number of patients with diabetes mellitus will double from the year 2000 to 2030, especially in developing countries (8). This 21st century pandemic of diabetes, added to the ageing of the population, arterial hypertension, and obesity is expected to significantly impact the prevalence of ESRD across the world and hence the needs of kidneys for transplantation.

CONSEQUENCES OF ORGAN SHORTAGE

The most important and obvious consequence of organ shortage is the fact that many patients will never be placed in the waiting list, and many will die or deteriorate while waiting for an organ. No less than 1 million people die every year in the context of ESRD without an adequate therapy all over the world (Luc Noel, personal communication).

Another important problem derived from shortage is the cost to the systems of the alternative renal replacement therapies to kidney transplantation, that is, dialysis. Lysaght (9) predicted the cost of dialysis in the world would be 1200 billions of US$ for the decade 2000 to 2010, probably underestimated. In Spain, Italy, and Western Europe in general, renal replacement therapy represents 2% to 2.5% of all health expenses. The total therapy cost per patient in dialysis per year in the European Union is approximately 50,000€ (U.S. $70,830).

Kidney transplantation has proven to have a more favorable cost effectiveness ratio than dialysis. It is related to better results in terms of survival (10) and quality of life (11). In addition, depending on the country, the cost of kidney transplantation can be offset in 2 to 4 years when compared with dialysis. This has been clearly proven in Europe or the...
United States, but also in countries as Pakistan, where renal transplantation remains being the best and least expensive renal replacement therapy (12, 13).

ORGAN SHORTAGE AND TRANSPLANT COMMERCIALIZATION

Desperation of patients waiting to be transplanted at a moment of organ shortage derives in another dramatic consequence, which is the development of criminal practices, as organ trafficking and the progressively better known phenomenon of transplant tourism.

Transplant tourism is defined as the movement of organs, donors, recipients, or transplant professionals across jurisdictional borders for transplantation purposes, when it involves organ trafficking and transplant commercialism or if the resources devoted to providing transplants to patients from outside a country undermine the country’s ability to provide transplant services for its own population (14). This phenomenon has emerged in the context of lack of organs as an immediate solution for patients in need and an extremely unequal distribution of wealth, with 20% of the population all over the world controlling 80% of global resources. Not by chance, the most usual practice is represented by the movement of patients from rich to poor countries, profiling a “North to South” flow in which wealthy patients, in their desperation for finding an organ, travel to developing countries where the donor, usually a vulnerable and poor person, agrees to sell a kidney to solve his also desperate economical situation (15).

These practices have also one of their main roots on results related to living kidney transplantation, in particular, which is related to better outcome results in terms of patient and graft survival than deceased kidney transplantation. Today, these better results are so regardless of the existing relationship between donor and recipient (16). Hence, living unrelated kidney transplantation has become a reality with excellent results after advances in immunosuppression have reduced the relative importance of human leukocyte antigen matching for posttransplant outcome.

Examples of these practices, that have arisen as a modern horror added to the endless series of tragic disasters that affect the whole world, are unfortunately too abundant. Asia, with 60% of the world population, provides no more than 2% to 3% of all deceased organ donors, leading to the proliferation of living transplants performed under the umbrella of different forms of commercialisation. India, Pakistan, Philippines, Egypt, and several Latin American countries are recognized as involved in organ trafficking and transplant tourism (15). In China, most of the transplanted organs were alleged to have been procured from executed prisoners (17), a practice which has been criticized by the international community, with a quite recent and fortunate compromise of the Chinese Government to stop this practice.

Another particular form of commercialization is the Iranian model (18). In this country, nearly 2000 patients receive a kidney transplant from a living donor every year, most of them from unrelated donors. Donors receive some bonus partially supported by the state and partly by the recipient, in a system which is organized and controlled by nongovernmental organizations and forbidden to foreign citizens. Although criticized by the international community, this system has allowed the country to finish with the kidney transplant waiting list and avoid transplant tourism and defendants claim that the system cannot be judged from the opulence of Occidental countries.

Organ trafficking and transplant tourism violate the most basic human rights. These practices are also related to safety problems especially in the case of the living donors, with no guarantee of application of the safety international standards, but also in many recipients transplanted by these means (15). These practices also cause a profound damage to the universal image of donation and transplantation, which generates a climate of distrust toward the system that might contribute even more to the exacerbation of the underlying problem of shortage of organs for transplantation.

GLOBAL APPROACH TO ORGAN SHORTAGE: THE ROLE OF TRANSPLANTATION SOCIETY, WHO AND ONT

Organ shortage and its consequences, including organ trafficking and transplant tourism, has become a universal problem to the point that the World Health Organization (WHO) estimates that at least 10% of all kidney transplants in the world are performed under some kind of commercialism. Universal problems need global solutions. It is in this context where the WHO, together with The Transplantation Society, some years ago initiated a global project to overcome global shortage and efficiently combat unethical practices. Actions as the recent generation and wide dissemination of the “The Declaration of Istanbul against transplant tourism and commercialism” (14), are good examples of this global approach. The Spanish Transplant Organization (ONT), an official Collaborating Centre of the WHO, is very actively participating in this process from the very beginning.

The mission of the WHO in the area of transplantation is to meet the requirements of the 57th World Health Assembly Resolution WHA 57.18, about Human Organ and Tissue Transplantation (19). Since 2005, WHO with the support of Transplantation Society and ONT started a set of consultations, two of a global scope, and several regional consultations with national health authorities in the different regions of the WHO. These regional consultations have been held in Manila with the countries of Western Pacific, in Karachi with Muslim countries, or in Slovenia with the Republics of the old Soviet Union, among others.

From the very beginning, the structure, background, stability, and experience of ONT were offered to the WHO to support a partnership in developing an International Observatory of Transplantation, a need that was to be covered through the Global Knowledge base on Transplantation (GKT), with four components. GKT1 and GKT2 led to the Global Observatory on Donation and Transplantation (http://www.transplant-observatory.org/default.aspx). This observatory, developed by ONT in collaboration with the WHO, is available since 2007 and provides an interface for health authorities and the general public to access data on donation and transplantation practices and legal frameworks all over the world.
The international role of Spain in this field is also the consequence of the successful donation program in this country, with the highest deceased donation rates ever described in the world and that double the mean value for the whole European Union. The success of the Spanish system is based on the implementation of a set of measures, mainly of organizational nature, that is internationally known as the Spanish Model of Donation and Transplantation (20). These measures followed the creation of ONT in 1989 and led Spain to triple the number of organ donors, from 500 to more than 1500 donors in 2007 and more than double the deceased donation rates, from 14 to 34 to 35 donors pmp (Fig. 2), resulting in significant reductions in the number of patients in the waiting lists and in the waiting times.

THE IBEROAMERICAN EXAMPLE

But it is in Latin America where the Spanish cooperation is becoming clearly important for obvious historical and linguistic reasons. Spain, in close cooperation with the Panamerican Health Organization, is in charge of the development of Resolution WHA 57.18 (19), through the “Iberoamerican Network/Council of Donation and Transplantation” (RCIDT).

The creation of the RCIDT was approved by the Heads of States and Governments at a summit held in Salamanca, Spain in 2005. ONT was led in charge of the permanent secretariat of this newly created organism. The mission of the RCIDT, composed by 21 Spanish and Portuguese speaking countries, is the development of the cooperation between its members in terms of organizational, legislative, professional training, ethical, and sociological aspects related to donation and transplantation of organs, cells, and tissues in Iberoamerican countries. The RCIDT considers organizational aspects as equally relevant to tackle with organ shortage and cooperation indispensable to achieve the maximum effectiveness of the systems.

Since its creation in October 2005, the RCIDT has held seven meetings at Mar de Plata (Argentina), Madrid (Spain), Montevideo (Uruguay), Punta Cana (Dominican Republic), Santiago de Chile (Chile), Havana (Cuba), and Mexico DF (Mexico). The group has generated 11 recommendations and consensus documents (Table 1) on relevant aspects on donation and transplantation.

Because training has been considered essential, one specific action developed by the RCIDT has been the development of a whole training program in donation and transplantation activities. Through this ALIANZA Master, professionals appointed by the different health ministries of Iberoamerican countries are trained as transplant coordinators in Spain. Training seeks to facilitate the translation of the Spanish Model to the Latin American reality. With a 2-month duration each edition, these selected professionals had a stage in the biggest Spanish hospitals, participate in a general coordination training course and in other specific courses relevant for their training, which are held in Spain during the time of the Master. They have to present a final written project before reaching the final degree of the Master. ALIANZA Master has been performed annually since 2005, and so far 182 professionals have been trained, all of them already working at their countries and many occupying positions of responsibility at a national level (Fig. 3).

In parallel to the ALIANZA Master, training courses on specific aspects of the process of deceased donation and transplantation have been held in several American countries in particular, a program on training of trainers on the communication of bad news in Argentina, Chile, Colombia and Central America, and the Caribbean. In the context of these programs, teams of monitors are being trained that will be able to develop courses at their own countries and in others within the region. Finally, courses on quality and safety in the management of tissue banks are also being developed, with wide acceptance and increasing demand, mainly in those countries of the Southern cone.

In addition, the running problems of organ trafficking

TABLE 1. Recommendations and other relevant documents generated by the Iberoamerican network/council on donation and transplantation

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<thead>
<tr>
<th>Recommendation Rec RCIDT 2005 (1)</th>
<th>on autologous cord blood banks</th>
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<td>Recommendation Rec RCIDT 2005 (2)</td>
<td>on the role and training of professionals responsible for organ donation (transplant donor coordinators)</td>
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<tr>
<td>Recommendation Rec RCIDT 2005 (3)</td>
<td>on the functions and responsibilities of a national transplant organization</td>
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<td>Recommendation Rec RCIDT 2005 (4)</td>
<td>on quality assurance programmes in the donation process</td>
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<td>Recommendation Rec RCIDT 2005 (5)</td>
<td>on the training plan for training professionals in donation and transplantation</td>
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<tr>
<td>Recommendation Rec RCIDT 2006 (6)</td>
<td>on solutions to organ shortage (phases of the deceased donation process-areas for improvement)</td>
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<td>Consensus Document</td>
<td>criteria to prevent the transmission of neoplastic diseases through transplantation</td>
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<td>Recommendation Rec RCIDT 2007 (7)</td>
<td>on guides for the quality and safety of cells and tissues of human origin for transplantation</td>
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<tr>
<td>Recommendation Rec RCIDT 2008 (8)</td>
<td>on bioethical considerations on donation and transplantation of organs, tissues, and cells</td>
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<tr>
<td>Recommendation Rec RCIDT 2008 (9)</td>
<td>on harmonization of criteria for the diagnosis of brain death in Iberoamerica Declaration against transplant tourism</td>
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and transplant tourism, which affect some of the countries within the region were raised at the last meeting of the RCIDT at Havana, in May 2008. Since its creation, the RCIDT has expressed its complete opposition to these practices, which facilitate transplant commerce and has considered them as morally condemnable. In this context, the relevance of the document on bioethical considerations produced by the RCIDT must be highlighted. Also, the RCIDT is providing specific support to those organizations in charge of the oversight of donation and transplantation in countries affected by these problems to better face them. This support has been documented at the Declaration against Transplant Tourism.

As a result of all this process and all the activities developed by the RCIDT:

- Donation and transplantation organizations have been created, restructured, or revived in countries, which lacked of this type of system or which activity was minimal or null. These organizations rely or are supported by the health authorities, following the Spanish model, and are being organized as a coordination network.
- Training activities for coordinators are being consolidated, through the ALIANZA Master and courses performed in Iberoamerica in cooperation with several countries. Training is being focused to the different areas within the region and tailored to their specific needs.
- Initiatives to harmonize criteria, in agreement with scientific societies and in accordance to international standards, are being developed, focused on a wide number of aspects, as diagnostic criteria for brain death or clinical evaluation criteria of the possible donors.
- RCIDT is progressively becoming a technical, ethical, training, and cooperative reference for the development of transplant activities in all the countries within the region.
- In addition, deceased donation activities are progressively increasing in countries within the region. The most notable change was detected from the year 2005 to the year 2006. In just one single year, deceased donation activities increased as much as 60% in Colombia, 30% in Cuba, 27% in Venezuela, 22% in Chile, 20% in Uruguay, or 11% in Argentina. Uruguay achieved during 2006 deceased donation rates close to those described in the United States (25.1 donors pmp).

**CONCLUSIONS**

In conclusion, organ shortage is a problem of a universal scope. It has important individual and global consequences. As a universal problem, it must be approached through global initiatives that provide the basic standards and pillars over which locally tailored actions are to be designed and implemented. Although changes in organ donation take time, what the Latin American experience shows is that, if steps are taken into the right direction, everything is possible, even the construction of a successful deceased donation program.

**REFERENCES**