
Reluctant acceptance of xenotransplantation in kidney patients on the waiting list for transplantation

Leonieke W. Kranenburga,*, Chantal Kerssensa, Jan N.M. Ijzermansb, Willij Zuidemac, Willem Weimarc, Jan J.V. Busschbacha

a Department of Medical Psychology and Psychotherapy, Erasmus University Medical Center, PO Box 1738, 3000 DR Rotterdam, The Netherlands
b Department of General Surgery, Erasmus University Medical Center, Rotterdam, The Netherlands
c Department of Internal Medicine-Transplantation, Erasmus University Medical Center, Rotterdam, The Netherlands

Available online 10 May 2005

Abstract

Previous research has shown contradictory results regarding the acceptance of xenotransplantation (XT) by kidney patients. This variance in attitude towards XT could be explained by differences in knowledge of XT, the availability of alternative treatment options, specific beliefs and cognitions of the patient, and differences in the health status of the patients. We studied 61 patients in this contention in the Netherlands waiting for a kidney transplant. All took part in in-depth interviews and filled out questionnaires on two occasions, once before and once after an information brochure on XT had been read. We found that a better health status is correlated with a greater acceptance of XT, but only before information was given. After information had been given, the acceptance of XT decreased significantly. However, if XT is the only possibility in a life-threatening situation, almost all patients are willing to accept XT, except for a small group (approximately 10–15%) with fundamental religious and/or spiritual objections against such treatment. When alternative treatment options such as a human cadaver donor, a living related donor or commercial donor are offered, the majority of patients would prefer those to XT. The main reason for reluctance is uncertainty about the risks of XT to personal health. Because alternatives are currently available, we expect that XT will become more popular only if future results of this procedure have proved to be comparable to transplantation with a human donor kidney.

Keywords: Xenotransplantation; Kidney patients; Information; Ethics; Organ donation; The Netherlands

Background

In the Netherlands, the average waiting time for a cadaver kidney transplant has increased to approximately four years. A future alternative that could shorten the waiting list is xenotransplantation (XT). However, XT is a controversial topic for medical (e.g., infection with porcine retroviruses), ethical (e.g., individual versus collective risk-problems) and psychological reasons (e.g., adjusting to lifelong lifestyle prescriptions). Studies investigating attitudes towards XT research and accepting xenografts have emerged in many countries over the past ten years (see the reviews...
of Mohacsi, Thompson, & Quine, 1998; Coffman et al., 1998; Julvez, Tuppen, & Cohen, 1999; Schlitt, Brun-khorst, Haverich, & Raab, 1999; Persson, Persson, Ranstam, & Hemeren, 2001; and Lundin & Idvall, 2003). However, research has shown ambiguous numbers regarding the acceptance of XT by kidney patients. Outcomes range from 78% that would accept a pig-organ in a British study (Ward, 1997), while results from Australia were much more modest (42%: Mohacsi, Thompson, Nicholson, & Tiller, 1997). It is difficult to see why these results differ so much, as in both studies written questionnaires were used that allowed for simple responses only without a clarification or motivation for the response. In the present study, we used both written questionnaires and a semistructured face-to-face interview to investigate these controversial findings. In particular, we investigated whether the attitude towards XT could be explained in terms of differences in knowledge of XT, the availability of alternative treatment-options, different belief systems and differences in the health status of patients.

Methods

Patients

We studied 61 patients on the waiting list for a kidney transplant (57% male). The mean age was 50. Thirty-eight patients (62%) were undergoing hemodialysis, 20 (33%) of the patients were treated with continuous ambulatory peritoneal dialysis and 3 (5%) were about to start dialysis. All patients treated with hemodialysis or continuous ambulatory peritoneal dialysis were on the waiting list for a kidney transplant, and the patients that were about to start dialysis were to be put on the waiting list in the near future (at starting dialysis). Of these 61 patients, 15 patients (25%) came to the transplantation unit of our University Hospital for the very first time, and 18 patients (30%) of these 61 had been transplanted before. Included were patients on the waiting list for a kidney transplant, or those to be put on the waiting list in the near future and those with sufficient mastery of the Dutch language. New patients were enrolled consecutively, and patients already treated with continuous ambulatory peritoneal dialysis or hemodialysis were randomly selected from the registry. Despite the inclusion criterion with regard to the Dutch language, only 34 patients (56%) were born in the Netherlands. The interviews took place at the faculty or the University Hospital, and occasionally at the patient’s home. The University Medical Ethical Review board has approved this study and informed consent was obtained from all patients. Notably, this study was conducted in 2002 and 2003, when the Dutch public became more aware of virally transmitted diseases. At this time, the epidemics of classical swine fever and mad cow disease were at their height and receiving a lot of media attention. A possible increase in awareness of viral risks might have influenced the responses of the patients.

Materials

All patients were seen twice: both meetings consisted of written questionnaires and an in-depth face-to-face interview. During the interview, participants had to fill out four exercises on their willingness to undergo XT. We aimed to address an effect of knowledge on attitudes by giving patients an information brochure after the first meeting. This brochure contained general information on kidney transplantation, and specific information on living kidney donation, cadaver kidney donation, commercial donation and XT. In this brochure it was clearly stated that law forbids commercial donation and that XT was not yet possible. The specific information focused in particular on (presumed) waiting time, (presumed) quality of the kidney and the risks for the persons involved. This brochure also contained information on lifestyle prescriptions for patients after XT (FDA guidelines on infectious disease issues in Xenotransplantation, 2001). Two weeks elapsed between the first and second meeting (M1 and M2, respectively). The anticipated increase in knowledge was measured by closed interview questions (e.g., Do you know which animal would be used for XT of the kidney?) and open interview questions (e.g., Why would they use that kind of animal?). A correct answer was scored as 1 (max = 8).

Health status was assessed using medical status data (i.e. kind of treatment, being transplanted before, and time on waiting list) and the EuroQol. The EuroQol consists of the EQ-5D (EuroQol 5 dimensions), a five-question health-related quality of life questionnaire, and the EQ-VAS, a visual analog scale (VAS) that indicates the subjective valuation of one’s health (Brooks, 2003). To investigate the willingness to undergo XT, we used four methods that differed in whether or not alternative treatment options were offered. We used a (waiting) time trade-off method, a VAS, statements (Mohacsi et al., 1997) and a ranking task. The purpose of the waiting time trade-off method is to find out how many years on the waiting list one is willing to trade for the immediate acceptance of XT. Our starting point was the question: “What would you choose; to undergo XT now, or to wait for four years for a kidney from a human cadaver donor ?” Depending on the answer, we added to or subtracted years from these four years. The period of four years was chosen as the starting point because it is the current average waiting time for a human cadaver donor (CAD) kidney in the Netherlands. In addition to this trade-off, we also asked patients if they would accept XT if it were the only option in a life-threatening situation. The VAS consisted...
of a 10 cm vertical line on which patients indicated their personal willingness to undergo XT (willing vs. not willing on either scale end). For the ranking task, patients ranked the following options: CAD, living related donor (LRD), XT and commercial donor (CD). The alternative “CD” was explained in its broadest sense as “someone who gets paid for his or her kidney”. We asked them: “Suppose that all four forms of transplantation were available, what would you in that case prefer first (second, etc.)?”

The semi-structured interviews started with the questions on knowledge, followed by the exercises on willingness to undergo XT. Special attention was given to the thoughts and motives underlying individual choices. Finally, the interview also included questions about the need for additional information about XT and anticipated support if it were to become an actual treatment option.

**Statistics**

To compare scores of the patients between measurements 1 and 2 (M1 and M2), we used the paired samples t-test, Wilcoxon signed ranks test and McNemar test. To compare variables or scores of subsamples within M1 and M2, t-tests for independent samples were used; α was set at 0.05.

**Results**

**Knowledge and information**

We observed a significant increase in knowledge about XT when the mean knowledge-scores on the first and second interviews were compared (M1 vs. M2, \( p < 0.001 \), paired samples t-test).

**Health status**

At the time of the first measurement, we found that high scores on the five individual dimensions of the EQ-5D, which indicates a poor health-related quality of life, were negatively related with the acceptance of XT as measured with the yes/no statements (independent samples t-test, \( p = 0.03 \)). Furthermore, we found that a shorter time spent on renal replacement therapy was related to the acceptance of XT (independent samples t-test, \( p = 0.03 \)). However, after information was given the relation between the acceptance of XT and health status disappeared.

**Willingness to undergo XT**

Given the current state of affairs, most patients (67%) would prefer to wait four years in order to receive a human cadaver kidney than to undergo XT. After information was given, significantly more patients preferred waiting for a human cadaver kidney (Wilcoxon signed ranks test, \( p = 0.02 \)). When XT would be offered as the only treatment option in a life-threatening situation, 80% of the patients were willing to undergo XT at the time of the first interview, a percentage that hardly changed upon the second interview. Willingness was also measured by a VAS and by statements. These methods also indicated a more negative attitude towards XT after information was given (resp. paired samples t-test and McNemar test, \( p = 0.03 \) and 0.02) (Table 1).

Fig. 1 shows the results for the ranking task, and illustrates that a LRD is, in general, the most popular alternative for patients at present. After that, patients prefer, respectively, a CAD, a CD and finally XT. A similar distribution of preferences was seen during the first and the second interviews.

<table>
<thead>
<tr>
<th>Statement</th>
<th>Percentage in agreement</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before information N = 61 (%)</td>
</tr>
<tr>
<td>I would accept xenotransplantation myself</td>
<td>67</td>
</tr>
<tr>
<td>I would accept an organ from an animal closely related to man (e.g., baboon/chimpanzee)</td>
<td>59</td>
</tr>
<tr>
<td>I would accept an organ from a species distant to man (e.g., pig/sheep)</td>
<td>64</td>
</tr>
<tr>
<td>I would accept an organ from a living relative</td>
<td>80</td>
</tr>
<tr>
<td>I would accept an organ from someone genetically unrelated but living (e.g., spouse)</td>
<td>82</td>
</tr>
</tbody>
</table>

*Statistical significant decrease in acceptance after information was given; McNemar test \( p < 0.05 \).
Motives for change of preference and reluctance to XT

Relevant in this respect is the group of patients that changed preference in favor of waiting for a human kidney after information had been given (13 patients, 21%). The explanations that accompanied their answers upon interview tell us that the change in preference does not necessarily reflect an attitude opposing XT, but rather reflects a cautious attitude to ‘choose the safest option’, having read and thought about XT in the period between interviews.

Another group (over half) of patients ranked XT last in both the first and second interview (Fig. 1). This group feared most the unknowns of XT and the possible risks, most often described as personal health risks. Beside this motive, these patients often reported feeling uncomfortable with the notion of having an animal organ.

Extreme motives

What were the main reasons for seven patients to say that they would never ever accept a pig’s kidney, both before and after information had been given? These patients had religious and other spiritual objections. They contended, for example, “If you take animal stuff you’ll become like that animal yourself”. And: “God created man and animal and there’s a border that cannot be crossed”. In explaining these objections, some patients referred to the Jewish or Islamic religions, which hold that pigs are impure animals. However, not all Muslim participants were unwilling to accept XT if it were a life-saving treatment option. There were five Muslim and no Jewish participants in our study.

By contrast, a group of 11 patients (18%) preferred XT instead of waiting 4 years for a human cadaver kidney on both measurement occasions. These patients found it emotionally less disturbing that the kidney would be from an animal rather than a human donor, or wished to be transplanted as soon as possible regardless of the source of the donor organ.

Identity

Nine patients (15%) felt that XT might change their personal identity, while seven (11%) were sure it would. Five of these seven patients stated they would rather die than to accept a pig’s organ.

Need for information and support

A large proportion of patients (85%) were interested in extra information about XT and/or support if XT were to become an actual treatment option. In particular, they would be interested in general information and what to expect in terms of medicine-use, survival rates of the porcine kidney and the results in terms of health status of previous patients who had undergone XT. Thirty-seven patients (61%) stated that they would like to have extra support if XT would become a treatment option. They especially would appreciate having the opportunity to talk to someone about what to expect after transplantation, and to receive emotional support (Fig. 2).

Discussion

The large increase in knowledge about XT after information was given may be explained by the fact that most patients knew little about XT when first interviewed. Therefore, an improvement in knowledge was relatively easy to attain. The results, which were obtained by various measurement methods, consistently showed an increased reluctance to accept XT after information had been provided. At that point, health status no longer related to the acceptance of XT. These findings foremost indicate that knowledge of the subject matter, in this case XT, is an important determinant of reluctance toward experimental treatments. In the absence of such knowledge (e.g., M1), other factors such as health status may affect reluctance. Before turning to a discussion of those factors, we wish to consider why health status no longer related to XT acceptance after information was given.

The finding that patients’ health status lost predictive value to XT acceptance at M2 could partially be explained by perceptions of possible gain. Typically, the perception of possible gain results from weighing the anticipated personal risks and benefits. This weighing
becomes difficult in medical frontline research, such as XT, since it is unclear what exactly is to be weighed (Lundin & Widner, 2000). In this study, the main reasons for changing preference in favor of waiting for a human cadaver kidney after having read XT treatment information were the unknowns of XT, or more specifically 'being unable to make or have an evidence-based judgment of the number and types of risks associated with XT'. We believe that an increased awareness of the risks associated with XT (i.e., perceptions of little/no gain) made patients apprehensive of XT treatment. As such, the explanation of possible gain underlines the impact that information may have on treatment decisions or acceptance. In explaining why both seriously ill and less ill kidney patients did not necessarily consider XT treatment beneficial after reading the information, we must assume that all perceived the risks to be considerable (or the gains to be marginal). If not, the perception of possible gain cannot satisfactorily explain why health status lost predictive value.

We also believe that an increased awareness of any risk, not just viral risks, will make a person more apprehensive of experimental treatments. It would be interesting and important in this respect for future studies in transplantation to address individual characteristics of patients, such as the willingness to take risks. Such characteristics may bear relevance to the acceptance of new, experimental treatments like XT.

Before information was given, we found that both better health status and shorter time spent on renal replacement therapy were related to acceptance of XT. Beside the fact that health status and time spent on replacement therapy are likely to be related, both findings could be interpreted in terms of weighing risks and gains, as suggested above. Patients who spent a shorter time on replacement therapy, on the one hand, gained a large reduction in waiting time if they were to undergo XT, compared to patients who have been on replacement therapy a few years already. Relatively healthy patients, on the other hand, arguably make decisions that promote becoming even healthier while relatively ill patients are more inclined to prevent their health from becoming worse. They are, in other words, more conservative in their perceptions of possible gain and hence preferred treatment options. A helpful framework in this respect is coping theory, in particular assimilative and accommodative coping strategies. Whereas the former evolves around previously set personal goals (such as working, having children, going abroad on vacation), the latter is all about accepting the current situation (dialysis) and adjusting old goals. It is well known from other illnesses, for instance chronic pain, that the assimilative strategy often precedes the accommodative strategy (Schmitz, Saile, & Nilges, 1996). Knowing this, it could be argued that relatively healthy patients employ an assimilative rather than accommodative coping strategy, and consequently are more willing to take risks and make unconventional decisions. Once more, it would be interesting and relevant in this respect to address a willingness to take risks in future studies of experimental treatment options. Besides being an individual characteristic that may explain differences between patients in similar circumstances, the willingness to make risky decisions could be an important confound of observed findings. We suggest, for example, that it is not necessarily health status per se that predicted XT acceptance in this study but rather an emotional state of mind. Such nuances may have large consequences for health professionals and the issues they target.

The one group that would not accept XT, under any circumstance, were patients with fundamental religious or other spiritual objections against XT. Although previous research indicated that religion is not a predictor of XT reluctance (Schlitt et al., 1999), our findings suggest that religion is a relevant factor. It is not necessarily the kind of religion someone adheres to, but rather the way religion is experienced. Some religious or spiritual beliefs were so strong that they seemed to relate...
directly to the contention that XT affects personal identity. Most patients, however, did not think that XT would influence their identity. In general, the attitude we observed was consistent with the ‘spare part view’ (Sanner, 2001), the idea that the body consists of several parts and that replacing one (in this case the kidney) for another does not change the person on the whole.

Despite the viewpoint taken by the monotheistic religions that donor organs are being viewed as purely functional and not affecting the recipients’ personal identity (Sykes et al., 2004), we found that this might not be experienced as such by individual adherents of a certain religion. A similar topic concerns the impureness of the pig for Islam and Judaism. Daar and Phil (1997) points out that despite there being a leeway to accept a pig’s organ for Jews and Muslims (since “need and necessity can allow that what is forbidden”), a minority opinion exists that pigs, because they are ritually unclean, cannot be used as source animals for organ transplantation. Indeed, this is what we found in our study. Two of the patients who stated that they would never accept XT did so on grounds of their Muslim religion.

We found that the percentage of patients that would accept XT varies with the availability of alternatives: 80–90% would accept XT if it were the last option in a life-threatening situation; 54–67% said ‘yes’ to the question ‘I would accept XT myself’ (presented amongst statements on other options); about 30% when it was offered as an alternative to waiting four years for a CAD; and finally <10% preferred XT to a CAD when it was offered amongst alternatives in a ranking task (forced choice method). The finding that a higher percentage of patients are willing to accept XT in a life-threatening situation is consistent with the conclusion of Persson et al. (2001). These findings suggest that attitude towards XT depends on the available treatment-options presented to the patients. This helps to explain the differences found in previous research: the study in which alternative treatment-options were presented (Mohacsi et al., 1997) resulted in a lower percentage of patients that would accept XT compared with the study that focused on XT alone (Ward, 1997).

Two critical comments can be made at this point. The first is a general comment on the need to invest into alternatives to cadaver transplantation. The ‘four years on the waiting list’ that we have used in our study is the average waiting time. Many patients will have to wait longer, while in the meantime their health status declines, and sometimes to the point where transplantation is not a feasible option anymore. The second comment refers to the interpretation of the results of the ranking task. In this exercise, the term “CD” was used. This term was explained in its broadest sense as “someone who gets paid for donating his or her kidney”. We found that the majority did not need further explanation of the term, since they dismissed the hypothetical option of a “CD” as unethical. However, further research could investigate whether a more refined distinction in various kinds of commercial donation influences the results of a similar ranking-task.

Conclusion

Providing information about a new, experimental medical treatment may inversely affect the acceptance of the treatment. In this study, information supported reluctance towards, rather than acceptance of, XT. Beside knowledge, patients’ health status can inversely affect acceptance of experimental treatments like XT. This may be related to individual characteristics and coping strategies rather than actual health status, however. The reluctance was unapparent when XT was offered as the only option in a life-threatening situation. In that case, most patients were willing to accept XT, except for a relatively small group with strong religious and/or spiritual objections. Since alternatives are currently present, the majority of patients are likely to prefer waiting for a human cadaver kidney than to accept XT treatment. Reluctance mainly stems from the unknown risks that are yet associated with XT, especially to patients’ personal health. If XT is ever to become of comparable risk to human donor kidney transplantation, its acceptance by kidney patients is likely to increase.

Acknowledgments

We would like to thank Professor Jan Passchier for initiating this research project and his continuing interest and suggestions. We would like to thank Dr. Medard Hilhorst for his valuable comments on this manuscript.

References


