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INVITED COMMENTARY

Adherence to immunosuppression: a critical aspect for the success of organ transplantation*

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Organ transplantation has made great strides in reaching its goal as a long-term replacement treatment for irreversible failed organs. However, a significant portion of grafts are lost as a consequence of nonadherence (NA) to immunosuppressants and agents treating co-morbidities.

In this issue of *Transplant International*, Leentje De Bleser and coworkers from Leuven, Belgium, address this important topic in heart, lung and liver transplant recipients. Comparing different methodological approaches and applying combined readouts, they provide a sensitive and alarming picture: 23.9–70% of transplant patients do not take their immunosuppressants as prescribed. Interestingly, lung transplant patients were less compliant than heart or liver transplant recipients in this study explained by the authors with a prolonged recovery after transplantation, younger recipient age and larger amounts of immunosuppressants and co-medications.

Although the clinical relevance of NA to medication and clinical appointments has been recognized for many years, imprecise definitions in addition to a lack of standardized methods make existing studies in this field difficult to compare. However, an estimated 20% of late acute rejection episodes and 16% of graft loss have been linked to noncompliance. Poor adherence by 1 year after transplantation has been identified as a significant risk factor for graft loss and patient death [1,2]. The death of one in ten liver transplant recipients has been linked to NA in a study of the Scottish database [3]. Besides, NA represents a significant economic burden for local transplant centers and national healthcare systems. In renal transplantation, NA increased medical costs by more than 12 000$ over a 3-year period, whereas the overall difference in medical costs between a poor compliant and a persistently highly compliant patient exceeded 33 000$ [2].

With its multifactorial and complex etiology, NA has been difficult to analyze and to target. Known risk factors for NA include younger age, psychiatric disorders, and patient's belief that medication is harmful and has considerable side effects. In a broader sense, cultural, social, and religious belief systems seem to play a role.

Economic aspects are of critical importance, particularly in countries without life-long support for

Figure 1 Adherence to immunosuppressants is critical in determining transplant outcome and is a burden and responsibility for patients, caregivers, and the healthcare system.

immunosuppressants, or, when significant co-pays have to be covered [2–5]. Other factors such as the geographic distance to the transplant center, illiteracy and the patient-physician relationship have been identified as risk factors [6]. It seems critical to identify those risk factors prior to transplantation to provide caregivers the opportunity for a more individualized care. Pretransplant self-reported NA, limited social support and, in some studies, higher education have been identified as independent predictors of post-transplant NA [7].

What can be done to improve adherence?

Studies on measurements to improve adherence in transplant patients are scarce (Fig. 1). Educational efforts and counseling during hospitalization demonstrated an improvement in compliance with immunosuppressants [8]. Simplifying daily regimens with single applications whenever possible may be of additional help.

Patient-related factors are critical and the motivation for adherence is based on transparency, education, motivation, and the confidence of being able to follow treatment [6]. A firm and trustful relationship of caregivers and patients throughout the transplant and recovery period and the reiteration of this relationship in addition to educational efforts during every hospitalization will support adherence: 'patients need to be supported, not blamed' [6]. Of note, oral rather than written information may improve compliance.

Of importance, with more elderly patients coming to transplantation, cognitive tests as part of the work-up may help to identify those with a limited comprehension of compliance to immunosuppressive treatment.

Long-term adherence to medication is critical also for the success in numerous other 'chronic' diseases. AIDS patients in the US, for example, have been teamed up with a 'patient care advocate' following up on them and bringing them to every appointment. This approach has greatly improved adherence in this patient population [9,10]. As a first step, a simple text message from the transplant center may help to remind patients of the correct intake and timing of their medication.

Finally, incomplete insurance coverage is a key factor for the adherence to immunosuppressants and other medications necessary after transplantation. Diverting from this concept with significant co-pays or even a discontinuation of coverage for immunosuppressants after a successful transplantation appear as *Penny-wise, Pound-foolish*, given the economic burden associated with noncompliance.

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