Original Research

A Comprehensive Review of Immunization Practices in Solid Organ Transplant and Hematopoietic Stem Cell Transplant Recipients

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ABSTRACT

Background: Vaccine-preventable diseases, especially influenza, varicella, herpes zoster, and invasive pneumococcal infections, continue to lead to significant morbidity and mortality in solid organ transplant (SOT) and hematopoietic stem cell transplant (HSCT) recipients.

Methods: We highlight guideline recommendations for the use of key vaccines in SOT and HSCT recipients and to review the latest evidence and developments in the field.

Results: Physicians should vaccinate individuals with end-stage organ disease, as vaccine seroresponse rates are higher pretransplantation. Most live attenuated vaccines continue to be contraindicated post-transplantation, but there are emerging safety profile and efficacy data to support the use of specific live attenuated vaccines, such as measles, mumps, and rubella in pediatric liver or kidney transplant recipients who are on low-level maintenance immunosuppression and without recent history of allograft rejection. An inactivated subunit varicella zoster virus vaccine is currently awaiting US Food and Drug Administration approval. While we await the safety profile and efficacy data of this subunit vaccine in transplant recipients, it will likely benefit immunocompromised individuals, including transplant recipients, because the live attenuated herpes zoster vaccine is currently contraindicated in transplant recipients and transplantation candidates receiving immunosuppression.

Conclusions: There is currently no evidence that vaccines lead to allograft rejection in SOT recipients. Household contacts of SOT and HSCT recipients should be vaccinated per the Advisory Committee on Immunization Practices schedule and recommendations.

Implications: Immunizations remain underutilized in transplantation patients. Although efficacy of vaccines in SOT and HSCT may be suboptimal, partial protection is preferred over no protection. (*Clin Ther*. 2017;39:1581–1598)

Key words: vaccines, immunizations, solid organ transplants, hematopoietic stem cell transplants, transplantation.

GENERAL PRINCIPLES OF IMMUNIZATIONS IN TRANSPLANT RECIPIENTS

Vaccine-preventable diseases, such as influenza and pneumococcal disease, still cause considerable morbidity and mortality in solid organ transplant (SOT) and hematopoietic stem cell transplant (HSCT) recipients. Although national and international guidelines advocate a systematic approach to pre- and post-transplantation immunizations in SOT and post-transplantation re-immunizations in HSCT recipients,[1–5] wide variations in immunization practices[6] and

Accepted for publication July 5, 2017.
http://dx.doi.org/10.1016/j.clinthera.2017.07.005
0149-2918/$ - see front matter

deviations from guidelines continue to occur in clinical practice, especially among HSCT recipients.[7]

Timing of immunizations is important in both SOT and HSCT recipients because administration of high doses of immunosuppressive medications in the form of induction immunosuppression in SOT recipients or conditioning regimen in HSCT recipients could result in an ineffective vaccine response in the early post-transplantation period. Waiting 2 to 6 months post-transplantation could lead to improved immunogenicity, though this guideline recommendation may be over-ridden in specific situations, such as an influenza outbreak.[1,2] In contrast to SOT recipients, who require lifelong immunosuppression, HSCT recipients eventually reconstitute their immune system with a few caveats: patients with graft-versus-host disease (GVHD) may experience prolonged periods of immunosuppression, which can lead to impaired responses to immunizations,[8] and even in the absence of GVHD, immune defects such as immunoglobulin G subclass deficiencies can persist. The emphasis in HSCT recipients is on an ordered sequence of re-vaccinations in the post-engraftment period.[3,4]

There are several challenges to immunizing transplantation patients. In SOT recipients, concerns have been raised about the impact of vaccination on the development of anti-graft alloimmunity or humoral alloimmune responses that could lead to graft rejection, specifically in association with influenza vaccination. Several large-scale studies have reported no increased risk of allograft rejection or dysfunction in influenza-vaccinated SOT recipients.[9–12] While Vermeiren et al[13] observed development of de novo anti–human leukocyte antigen antibodies after influenza vaccination in their cohort of SOT recipients, only 1 patient (1 of 169; 0.006%) developed donor-specific antibodies. Vermeiren et al concluded that the influenza vaccine is tolerable and SOT recipients receiving the influenza vaccine did not experience humoral alloimmune responses. In addition, although the levels of protection achieved by immunizations in the post-transplantation recipient may not always be optimal, it is still important to immunize in accordance with current guidelines, as partial protection is preferred to none. Finally, the types and doses of immunosuppressive agents administered may have an effect on vaccine immunogenicity. Studies have found that mycophenolate use was associated with decreased seroresponses to influenza vaccine in kidney transplant recipients in a dose-dependent fashion.[14,15] Other studies, however, found no difference in responses to influenza vaccine in kidney recipients who had received thymoglobulin versus basiliximab induction.[16]

IMMUNIZATIONS IN SOLID ORGAN TRANSPLANTATION CANDIDATES

Solid organ transplantation candidates are more likely to develop vaccine-induced immunity compared with SOT recipients receiving immunosuppressive agents. Physicians who provide care to potential transplantation candidates should vaccinate them in accordance with published guidelines as early as possible in the course of their end-stage organ disease.[1,2,5] The pre-transplantation evaluation is a convenient time to review immunization records and initiate these immunizations,[1,2,5] guided by screening serologies obtained at that time. Here, we will review the individual vaccines against viral and bacterial infections (Table I).

Yearly seasonal influenza vaccine is very important. In patients with advanced organ failure, influenza can be clinically severe, predispose to subsequent bacterial infection(s), and may delay transplantation. Current guidelines recommend the standard injected, inactivated influenza vaccine.[1,2] Further evidence is awaited regarding whether a higher-dose vaccine (that contains 4 times the amount of antigen contained in the regular inactivated influenza vaccine) or if the quadrivalent flu vaccine is superior in this population. Influenza vaccine should also be administered to all family members, close contacts, and health-care workers to provide herd immunity.[1,2]

Hepatitis A vaccine should be considered in all seronegative organ transplantation candidates, but given the increased risk of severe hepatitis A infection in patients with underlying liver disease, it is particularly important in liver transplantation candidates. Hepatitis B vaccine is important for patients who lack anti–hepatitis B surface antibody, because hepatitis B acquisition in the post-transplantation period has been reported, especially in the setting of donor-derived hepatitis B virus (HBV) infection as a result of accepting an allograft from a donor with positive anti–hepatitis B core antibody.[17–19] The 3-dose HBV vaccine series (0, 1, and 6 months) is most commonly administered to seronegative patients, although the third dose may be given post-transplantation if the transplantation occurs in the interim. Accelerated regimens (eg, 0, 1, and 2 months, or 0, 7, and 21–30 days) have been advocated by some clinicians in