REVIEW

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Primary Care of the Transplant Patient

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ABSTRACT

A total of 153,245 patients are living with a solid organ transplant in the US. In addition, patients are experiencing high 5-year survival rates after transplantation. Thus, primary care physicians will be caring for transplanted patients. The aim of this review is to update primary care physicians on chronic diseases, screening for malignancy, immunizations, and contraception in the transplant patient. Several studies on the treatment of hypertension and hyperlipidemia demonstrate that most agents used to treat the general population also can be used to treat transplant recipients. Little information exists on the medical management of diabetes in the transplant population, but experts in the area believe that the treatment of diabetes should be similar. Transplant recipients are at increased risk for all malignancies. Aggressive screening should be employed for all cancers with a proven screening benefit. Killed immunizations are safe for the transplant population, but live virus vaccines should be avoided. Women of childbearing age should be counseled about the impact of immunosuppressants on the efficacy and side effects of contraception.

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The 2006 annual report of the Scientific Registry of Transplant Recipients shows that by the end of 2004 there were 153,245 individuals living with a transplant in the US. In 2005, 16,072 individuals received a kidney transplant and 6000 received a liver transplant. Over 2000 individuals received a heart and 1400 received a lung transplant in the same year. As of 2005, there were over 89,000 individuals waiting for transplantation.[1] The survival rate for transplant recipients is high. Unadjusted 5-year survival rates for living donor renal and liver transplant recipients are 90% and 77%, respectively, while heart recipients' 5-year survival is 74%.[1] Because so many transplant recipients survive beyond the initial postoperative period, they are presenting to primary care offices in increasing numbers. Primary care physicians need to be prepared to evaluate and treat transplant recipients.

The primary care physician has the potential to play a major role in the prevention of illness and death for the transplant population. Among transplant recipients who have survived for at least 3 years after transplant, the cause of death is malignancy for 24% and complications of cardiovascular disease for 21%.[2] A large component of the primary care physician's activities revolve around early detection of malignancy and prevention of cardiovascular disorders. Thus, primary care physicians need to be experts in the special attributes of malignancy and vascular disease in transplant patients.

The goal of this review is to assist the general internist or family physician to provide primary care for transplant recipients. Initially, the immunosuppressants commonly used in transplant medicine are reviewed. The care of hypertension, hyperlipidemia, and diabetes is then discussed. Lastly, screening for malignancies, contraception care, and proper immunization practices are reviewed.

THE IMMUNOSUPPRESSANTS

Primary care physicians should have a working knowledge of the common immunosuppressants employed for the solid organ transplant population. These medicines have the potential for multiple side effects as well as interactions with medicines commonly prescribed in a primary care practice.

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The immunosuppressants used in transplant medicine include corticosteroids, cyclosporine, tacrolimus (FK506), sirolimus, azathioprine, and mycophenolate mofetil. A thorough discussion of the impact of corticosteroids on primary care practice is beyond the scope of this article and has been addressed previously.[3-7] Cyclosporine and tacrolimus are the most common immunosuppressants used in transplant medicine.[8-10] These calcineurin inhibitors and sirolimus are metabolized through the cytochrome P450 system, causing interactions with many medications employed in primary care. Medications that are metabolized through the same system (Tables 1, 2) can accelerate or decelerate the metabolism of these immunosuppressants, leading to either toxic or sub-therapeutic levels. Azathioprine and the newer immunosuppressant mycophenolate mofetil are purine synthesis inhibitors. They are not metabolized through the cytochrome P450 system and do not have as many problems with interactions.[11]

CLINICAL SIGNIFICANCE

- Primary care physicians provide long-term care for organ transplant recipients.
- Most antihypertensive and lipid-lowering therapies can be used in the transplant recipient.
- Aggressive screening should be employed for all cancers with a proven screening benefit.
- Live virus vaccines should be avoided, but killed vaccines are safe.
- Women of child-bearing age should be counseled that immunosuppressants affect contraception.

HYPERTENSION

The prevalence of hypertension is increased in transplant recipients compared, with the general population. Among liver transplant recipients, the prevalence is 55%-85%. Renal recipients and heart recipients have a prevalence of up to 90% and 100%, respectively.[12-14]

The pathophysiology of hypertension in transplant recipients is not fully understood, but is mediated through the use of immunosuppressants. Calcineurin inhibitors are known to increase the release of endothelin, leading to constriction of the afferent renal arteriole and a decrease in the glomerular filtration rate. This results in an expansion of the intravascular volume and an associated elevation in systemic blood pressure.[13]

The National Kidney Foundation Kidney Disease Quality Outcomes Initiative and the American Society of Transplantation have published guidelines for assessment and management of hypertension in patients who are transplant recipients. The appropriate target for blood pressure control in renal and liver transplant recipients is $<130/<80$ mm Hg.[12,15]

Several randomized controlled studies address treatment of hypertension in the transplant recipient.[14,16-25] The following classes of antihypertensives have been shown to be effective in this population: calcium channel blockers, angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, beta-blockers, and diuretics. No single class of drugs has been shown to be more effective. Primary care physicians should consider the following in choosing an antihypertensive regimen. First, one should consider the transplant recipient's comorbid conditions in choosing an antihypertensive regimen. Angiotensin-converting enzyme inhibitors and angiotensin receptor blockers are preferred in the presence of microalbuminuria or diabetes. Second, the pathophysiology of hypertension in transplant recipients should be considered. Theoretically, calcium channel blockers would be an appropriate agent for this group of patients because of their ability to counteract afferent arteriolar vasoconstriction. Diuretics would help to reduce volume expansion. Lastly, primary care physicians should consider drugs that reduce the cost of immunosuppressants. When calcium channel blockers such as diltiazem are used, cyclosporine, tacrolimus, and sirolimus levels increase, allowing for less costly lower doses of the medications.

Table 1 Medicines that Increase the Risk of Rejection in Transplant Recipients on Calcineurin Inhibitors

Antiseizure medicines
Phenobarbitol
Phenytoin
Carbamezipine
Antimicrobials
Isoniazide
Nafcillin
Substances
Tobacco
Marijuana

HYPERLIPIDEMIA

Hyperlipidemia is a common problem among transplant patients. Six to 12 months after liver transplantation, total cholesterol increases by 20%-43%, triglycerides increase by 38%-56%, and high-density lipoprotein is reduced by 50%.[26-29] The prevalence of hyperlipidemia for renal and heart transplant recipients is 90%[30-33] and 64%, respectively.[34]

The pathophysiology of hyperlipidemia in transplant recipients is multifactorial. Major factors include pretransplant lipid levels, weight gain that commonly occurs after transplantation, diabetes mellitus, and hypothyroidism. Immunosuppressants and medications used to treat hypertension also contribute to