ACE Anesthesiology Continuing Education

ACE Question

Which of the following immunosuppressive drugs is MOST likely to cause renal dysfunction?

(A) Tacrolimus (B) Mycophenolate mofetil (C) Basiliximab

Immunosuppressant drugs are used to prevent or treat allograft rejection. Most of these drugs act during the induction phase of the immunological response, reducing lymphocyte proliferation. Some of them are also used in the maintenance phase. There are three main groups based on the site of action: interleukin-2 (IL-2) production or action, cytokine gene expression, or purine or pyrimidine synthesis. Complications of chronic immune suppression drugs are shown in the Table.

Tacrolimus is a macrolide antibiotic with an action very similar to that of cyclosporine. However, it is more potent and has a shorter half-life. It blocks the action of calcineurin, leading to reduction in various transcription factors and IL-2 expression, primarily in T-helper lymphocytes. Tacrolimus can lead to renal toxicity due to afferent arteriolar vasoconstriction and the subsequent reduction in glomerular filtration rate (GFR). Decreasing the dose of tacrolimus can reverse GFR reduction and renal toxicity. Tacrolimus therapy has also been associated with hypertension and neurotoxicity.

Mycophenolate mofetil restrains the proliferation of both T and B cells by inhibiting de novo purine synthesis in these cells. It may be associated with adverse gastrointestinal effects, but it is not as likely as tacrolimus to cause renal dysfunction.

Basiliximab is a chimeric monoclonal antibody to CD25 and an IL-2 antagonist. It is used as an alternative or in addition to steroids for the induction of immunosuppression in solid organ transplantation. It has a relatively safe profile. No cytokine release syndrome has been associated with this drug, but anaphylactic reactions can occur. Basiliximab is unlikely to cause renal dysfunction. ■

References:

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4. Kaplan JA, Augoustides JGT, Manecke GR Jr, Maus T, Reich DL, eds. *Kaplan's Cardiac Anesthesia for Cardiac and Noncardiac Surgery.* 7th ed. Elsevier Saunders; 2017:1506-1507.

Answer: A

Table: Complications of chronic immune suppression

System	Adverse Effect	Associated Drug(s)
Central and peripheral nervous	Lowered seizure threshold	Tacrolimus, cyclosporine
	Peripheral neuropathy, encephalopathy	Tacrolimus
Cardiovascular	Hyperlipidemia	Sirolimus
	Hypertension	Cyclosporine
	Diabetes	Steroids, tacrolimus
	Atherosclerosis	Cyclosporine, tacrolimus
Renal	Renal insufficiency	Cyclosporine, tacrolimus
	Decreased glomerular filtration rate	Cyclosporine, tacrolimus
	Hyperkalemia, hypomagnesemia	Cyclosporine, tacrolimus
Hematologic	Infection	Significant potential with all agents
	Malignancy	Muromonab-CD3, antithymocyte globulin
	Thrombocytopenia	Azathioprine, mycophenolate mofetil
	Anemia	Azathioprine, mycophenolate mofetil

Information from Tepperman E, Ramzy D, Prodger J, et al. Surgical biology for the clinician: vascular effects of immunosuppression. *Can J Surg.* 2010;53(1):57-63, and Miller LW. Cardiovascular toxicities of immunosuppressive agents. *Am J Transplant.* 2002;2:807-18. doi:10.1034/j.1600-6143.2002.20902.

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Executive Report: 5 Impactful Trends

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published in *Anesthesiology* in February 2020 summarized current literature and cited uses in managing depth of sedation, adverse event/complication prediction, and management of OR logistics (*Anesthesiology* 2020;132:379-94). It is doubtful that AI will replace anesthesiologists, but rather potentially support and strengthen their roles.

Several simultaneous trends are pointing to the future of remote care. These include the use of telemedicine and remote monitoring coupled with the acceleration of ambulatory surgery and at-home recovery. Telemedicine grew in use during the pandemic and is now becoming more common in medical care. For anesthesiology, its potential in preop assessment and follow-up care appears clear. For a baby boomer looking at both my routine medical care and potential surgery, the possibility of recovery at home is viewed as more comfortable and cost-effective.

"The Shape of Things to Come" (novel by H.G. Wells)

These trends and more are a great challenge, but also a great opportunity for the specialty. I hold abundant optimism for anesthesiology. Having worked in health systems and in other medical specialties, I see anesthesiologists as uniquely qualified to lead in these turbulent times. Indeed, leadership is already evident in the range of skills (quality and safety, systems thinking, diplomacy) that anesthesiologists bring to their work every day, the numbers of members who have assumed leadership positions, and the number of issues that, collectively, this specialty has been called upon to lead. ■

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