Effects of Pranlukast on Vascular Endothelial Growth Factor Levels in Asthma

To the Editor:

We thank Dr. Medford for an interest regarding our study.1 There has been a clinical interest in the use of leukotriene receptor antagonists (LTRAs) in asthmatic patients who have already been treated with inhaled corticosteroids. However, a further benefit in symptoms and lung function from therapy combining LTRAs and inhaled corticosteroids is contrary to this finding. In this study, we found that pranlukast administration added little efficacy to inhaled corticosteroid therapy for reduction in vascular endothelial growth factor (VEGF) levels in induced sputum from asthmatic patients. However, it is possible that the trends toward reduction in airway VEGF levels after pranlukast administration in steroid-treated asthmatic patients might have reached statistical significance if more patients had been included in our study.

The mechanism of the reduction in airway VEGF levels in asthma induced by pranlukast administration is unclear. One report2 has indicated that asthmatic patients exhibited a greater expression of VEGF receptors (flt-1 and flk-1) in the airway mucosa. Moreover, increased VEGF expression in asthmatic patients were identified by infiltrating inflammatory cells in the submucosa in order of abundance in CD34+ cells → eosinophils → macrophages → T cells → mast cells. Therefore, one possible explanation is that pranlukast administration decreased airway VEGF levels via the reduction of infiltrating inflammatory cells. We also think that analysis of cell-associated VEGF isoform expression (VEGF164 and VEGF206) is important to understand VEGF bioactivity in asthma. Though the results were not shown in our study, we examined cell-associated VEGF isoform expression by immunohistochemical analysis. On the basis of these results, we found a significant correlation between the expression of free VEGF and that of cell-associated VEGF. In our recent study,3 we determined that the interaction between airway microcirculation and VEGF may be a key element in the pathophysiology of asthma. Therefore, pranlukast administration might decrease airway microvascular permeability through, at least in part, a decrease in airway VEGF levels in asthmatic patients.

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Atrial Fibrillation, Atrial Flutter, or Both After Pulmonary Transplantation

To the Editor:

We read with interest the recent report of Nielsen et al (August 2004).1 This is an important study that addressed the prevalence and predictors for atrial arrhythmias after pulmonary transplantation (PT). Nevertheless, some points should be reviewed due to possible misinterpretation.

Atrial fibrillation and atrial flutter were grouped together and termed “AF” in the results and analysis in the present study. However, it should be noted that they are mechanistically and therapeutically different entities, which should not be grouped under the same term.2 Atrial flutter is defined as macroreentry around one or more atrial anatomic obstacles (commonly, the tricuspid annulus or surgical incisions), which can be abolished by catheter ablation.3 A high incidence of atrial flutter has been reported in patients with PT.4 Atypical atrial flutter following PT is thought to be secondary to macroreentry around the anastomosis between the left atrium and pulmonary veins.6 On the other hand, the final etiologic mechanism of atrial fibrillation is unknown, and the best treatment for it is unclear. Electrical isolation of the pulmonary veins and the surrounding left atrium myocardium leads to atrial fibrillation abolishment in many patients.7 A similar electrical situation occurs in PT, in which the donor pulmonary veins and the surrounding left atrium tissue are not electrically connected to the recipient’s atria.

Therefore, current scientific evidence makes atrial flutter rather than atrial fibrillation more likely to occur after PT. Thus, separate descriptions and analyses of the incidence and predictive factors of these two different arrhythmias should have been performed in this study, and this warrants further investigation.

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To the Editor:

We appreciate the comments by Lazaro and colleagues regarding our recent article (August 2004). The authors suggest that our work would benefit from a separate analysis of patients with atrial fibrillation from those with atrial flutter (both grouped under the term AF in our study). They cite differences in the etiology of atrial fibrillation and flutter as to why a separate analysis would be useful. Unfortunately, little is known mechanistically about the development of atrial dysrythmias after lung transplant. Furthermore, both atrial fibrillation and flutter were observed in some patients in our study at different times postoperatively. Thus, trying to dichotomize all our patients into one category or the other would be difficult. We agree that future studies of the lung transplant population should include more detailed ECG and electrophysiologic monitoring, in order to better understand the mechanisms of atrial fibrillation and flutter in this population. We would emphasize, however, that AF, as defined in our analysis, is appropriate and clinically meaningful because we demonstrated specific risk factors and associations with clinical outcomes using this definition in a large cohort of lung transplant recipients.

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PHYSICIAN INTERACTION WITH INTERNET PHARMACIES IS RISKY

To the Editor:

Florida physicians who fill prescriptions for patients who seek medication via Internet pharmacies are at significant risk in the State of Florida. Florida law requires that a proper doctor/patient relationship exist before a Florida physician can prescribe legend drugs via the Internet. Florida Tele-Medicine Regulations, 64B8–9.014, F.A.C. (2003) require, among other things, a history and physical and a discussion to occur between the physician and the patient regarding treatment options and the risks and benefits of treatment prior to prescribing legend drugs to patients through the Internet, telephone, or facsimile. Florida law also requires, as always, the creation and maintenance of contemporaneous medical records by the physician.

A new Florida statute effective this year also specifies, in part, that: (1) any Internet pharmacy that dispenses drugs to Floridians must obtain a permit, (2) dispensing drugs to Floridians without a permit after July 2004 is a felony, and (3) pharmacies and pharmacists must ensure that a proper physician/patient relationship exists before filling a prescription. Additionally, Florida physicians should be aware of appropriate Drug Enforcement Administration guidance on the topic. For instance, Federal law also requires the existence of a bona fide doctor/patient relationship.

The risk of violation in Florida is not merely theoretical. It is real. For instance, in June 2004, a Final Order was entered into the case of Department of Health v. Serge Lefevre Alexandre. Dr. Alexandre was fined $10,000, required to pay $18,000 in Department of Health costs, required to perform 50 h of community service, and obtain an additional 10 h of continuing medical education arising out his violation of the law. The pertinent facts in that case are as follows: (1) a patient in Texas logged onto an Internet pharmacy and selected doxycycline, a legend drug; (2) the Web site contained a “Consent Medical Care” questionnaire, which the patient completed; and (3) based on the patient’s completion of the form, the doctor prescribed the doxycycline, and the prescription was filled at a Florida pharmacy.

The doctor never personally interviewed or examined the patient, nor did he ever rely on information provided by another qualified medical professional who had personally interviewed and/or examined the patient. In fact, the doctor had no communication of any kind with the patient other than interaction via the Internet Web pages. Under these circumstances, the Board found that the doctor failed to establish a proper physician/patient relationship. The Board was helpful, however, in clarifying that the following is required under these circumstances: (1) a personal interview between the physician and patient via a mode of communication that is controlled by the doctor or a “Qualified Medical Professional,” and (2) an examination if necessary by the physician or the qualified medical professional. A “Qualified Medical Professional,” according to the Board of Medicine, means a licensed physician, nurse practitioner, or physician’s assistant.

Moreover, the Board stated that it was necessary for the doctor’s medical records to contain adequate evidence that the physician/patient relationship had been developed, that an adequate medical history had been taken, that the physician had made a diagnosis, and that the physician had developed an adequate treatment plan. None of these things were present in the case before the Board.

In truth, Dr. Alexandre’s punishment was fortunate since the Board revoked a physician’s license a couple of months earlier under similar circumstances. Florida physicians should take great care to ensure they comply with applicable law when dealing with Internet pharmacies. Merely relying on an Internet questionnaire and/or even an interview by someone who is not a Florida physician may expose Florida doctors to significant risk and penalties.

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