IV Epoprostenol in Gaucher's Disease

To the Editor:

We read with interest the article by Bakst et al (October 1999), reporting the use of continuous IV epoprostenol in a patient with Gaucher's disease with pulmonary hypertension. The effective use of this therapeutic modality is encouraging. Pulmonary hypertension in patients with Gaucher's disease may be secondary to the effects of interstitial lung involvement or intercapillary plugging by Gaucher cells, or primary-like, in association with enzyme replacement therapy. Enzyme therapy may ameliorate pulmonary disease, including improvement in secondary pulmonary hypertension, as was initially observed in the cited case. Later reappearance of pulmonary hypertension may be associated with enzyme treatment.

We have a similar case of a 34-year-old woman who had undergone splenectomy, who presented with hypoxia and a tricuspid incompetence (TI) gradient of 27 mm Hg. After 3 years on enzyme therapy with improvement in hypoxemia, clubbing, and pulmonary function tests, the TI gradient dropped to 20 mm Hg (within the normal range). After 2 more years of treatment, she developed elevation of TI gradient to 37 mm Hg. We also documented another patient with Gaucher's disease, who started enzyme therapy with a TI gradient within the normal range, which then rose above 30 mm Hg with treatment with the placental derivative, alglucerase, and then returned to the normal range after withdrawal. Challenge with the recombinant form, imiglucerase, resulted in elevation of the TI gradient above 30 mm Hg, and treatment withdrawal again resulted in return to the normal range.

Continued use of enzyme replacement (and in very high dosage) in the case by Bakst et al could have been the cause of the reemergence of pulmonary hypertension, and enzyme withdrawal might be considered to wean her from lifelong dependence on epoprostenol. On the other hand, the success of epoprostenol may be of greater importance to patients who have other life-threatening features of Gaucher's disease and who cannot, therefore, terminate enzyme therapy. We applaud the pioneering efforts of Bakst et al, as like them, we are concerned with the increased number of patients with Gaucher's disease who develop pulmonary hypertension. In addition, we concur that echocardiography should be included in routine follow-up of all Gaucher patients, treated and untreated, despite the fact that, in recent guidelines for diagnosis and monitoring by the International Collaborative Gaucher Group registry, this procedure was unfortunately omitted.

Deborah Elstein, PhD
Ari Zimran, MD
Shaare Zedek Medical Center
Jerusalem, Israel

Correspondence to: Ari Zimran, MD, Shaare Zedek Medical Center, P. O. Box 3235, Jerusalem 91031; Israel; e-mail: zimran@md2.huji.ac.il

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Corticosteroid Therapy in Acute Asthma

To the Editor:

We read with interest the meta-analysis by Rodrigo and Rodrigo (August 1999) evaluating 16 randomized control trials on the effect of steroids in acute asthma. Their conclusion, based on effect size (ES) estimates of pulmonary function, was that systemic steroid effects do not seem to manifest themselves until ≥ 6 h after use. This is consistent with what is known about the time course of steroids in asthma, including our evaluation of IV steroid effects at 1 h. We recently finished evaluating the effect of IV steroids in acute asthmatic patients over 2 h using a randomized, double-blind, placebo-controlled trial, and noted a significant increase in peak flow measurements in the steroid group over 2 h. The ES estimate of peak flow was small, however, at 0.32 at the 2-h time point, when adjusting for baseline peak flow rates. It was unclear from their methods section how the 95% confidence intervals were calculated, or what standard error was used, so we could not include them here.) This ES of 0.32, assuming normality, suggests that the average asthmatic patient’s peak flow in the steroid group would be > 62% of the peak flows of asthmatic patients in the control group. Assuming this a study of high quality as graded by Rodrigo and Rodrigo, this result probably would not have changed their conclusion due to the small ES estimates for the other studies using systemic steroids under 6 h. It is unclear to us why their study showed a slight
improvement in peak flow with steroids at this time point. Possibilities include an unknown confounder that theoretically was controlled for during randomization, but can have an effect with small sample sizes, a postrandomizationselection bias of some type that we did not detect, chance, and the possibility that we actually found a steroid effect at 2 h.

One strength of our study that is not followed in other asthma studies was the recruitment of patients with acute asthma who had a poor peak flow response after one nebulizer treatment with albuterol. This excluded the subset of patients who have a poor peak flow response after one nebulizer treatment with steroids was the recruitment of patients with acute asthma who we actually found a steroid effect at 2 h. Some type that we did not detect, chance, and the possibility that we actually found a steroid effect at 2 h.

increased our chances of finding a difference in peak flow response between treatment and control. This is another possibility for our study findings compared to others. We congratulate Rodrigo and Rodrigol for their evidence-based effort. Despite our possible finding, the weight of the evidence reveals no effect of systemic steroids in improving pulmonary function in patients with acute asthma in the first 6 h. Even if our finding turns out to be real, the effect on improving pulmonary function compared to standard therapy would probably be marginal.

Gene R. Pesola, MD, MPH
Robert Y. Lin, MD, MS
Richard E. Westfal, MD
St. Vincent’s Hospital & Medical Center
New York, NY

REFERENCES

Infusion Phlebitis in Patients in a General Internal Medicine Service

To the Editor:

In relation to the recent article by Monreal et al., we believe readers may be interested to learn of the results of a study carried out in our General Internal Medicine Service and communicated at the International Symposium on Thromboembolism held in Lisbon in June 1999. In this work, we investigated the local complications of IV therapy in the 363 patients to whom it was applied in the Service over a period of 3 months, with emphasis on the frequency of phlebitis following venous catheterization and the risk factors favoring this complication; only first catheterizations were considered. Twenty-gauge catheters were used in 92% of cases, 22-gauge catheters in 3%, and 18-gauge catheters in 1.9%; needles were used in 1.7%, and in the remaining 1.4% of cases, central catheters were installed.

Phlebitis arose in 35% of cases. Monreal et al observed a slightly higher incidence, 39%, possibly because their study was limited to pneumonia patients and thus to patients receiving IV antibiotics, a known risk factor (see below); other authors have reported incidence rates from 20 to 70%. Onset was invariably within the first few days of catheterization (95% confidence interval, 2.7 to 3.5 days). There were no statistically significant differences among the different types of catheter (unsurprisingly, in view of the great predominance of 20-gauge catheters). Like Monreal et al and others, we found that IV administration of antibiotics was the greatest risk factor. Furthermore, risk increased with the number of antibiotics administered. Also like Monreal et al, we found that incidence was lower among patients who were receiving IV corticosteroids than among those who were not, with similar findings for diuretics and bronchodilators, although in none of these cases was the difference statistically significant. We regret not having investigated the influence of hemoglobin level, the pro-phlebitic effect of which was the most interesting finding of Monreal et al.

In conclusion, we found a high incidence of phlebitis among patients receiving IV medication. There appears to be no doubt that IV administration of antibiotics is a risk factor, and the risk increases with the number of antibiotics administered. Possible prophylactic measures include the use of heparin and limitation of the level of insult by control of drug dilution and infusion rate.

A. Pose-Reino, MD
J. M. Taboada-Cotón, MD
D. Álvarez, MD
J. Suarez, MD
L. Valkés, MD
Santiago, Spain

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