Systemic Corticosteroids in Stable Chronic Obstructive Pulmonary Disease

Do They Work?

D espite more than 30 years of clinical use and research, the value of systemic corticosteroids for patients with stable chronic obstructive pulmonary disease (chronic bronchitis and/or emphysema) remains uncertain. The controversy over steroid efficacy began in the 1950s with disagreements found in reports of early case series and observational cohort studies, and the dispute still has not been resolved because randomized trials have continued to reach conflicting conclusions. As of this writing, 14 studies of therapy with systemic steroids in stable chronic obstructive pulmonary disease have been performed as double-blind randomized clinical trials (RCTs), a design which is widely regarded as the most reliable way to evaluate therapy. The results of these trials differ. Overall, eight of the 14 trials show that systemic corticosteroids produce some measured benefit, whereas six trials report no effect. Of the 13 trials that examined FEV₁, an outcome event, six show greater improvement with steroids than with placebo, and seven do not. Two of the four trials that measure exercise tolerance (12-minute walk distance in three and treadmill exercise performance in one) show improvement following steroid therapy, whereas two do not.

As a result of these basic disagreements among the available RCTs, confusion about steroid efficacy is understandable, but interested clinicians will look for strategies to resolve this conflict. Of the available strategies for resolving conflicts in the literature, ie, informal review (which combines the literature with personal clinical experience); formal pooled analysis (in which data from all available studies are combined and re-analyzed as a single data set); and methodologic "meta-analysis" (in which the design and conduct of each trial is evaluated to identify the most reliable study), "meta-analysis" has proven useful to clarify several clinical controversies, including the role of steroids in stable COPD. Specifically, by crediting trials that used a crossover design with a washout (to assure optimal matching of compared groups and study conditions), we identified a subset of eight better-designed trials. By also requiring trials to assure that patients were stable at baseline (to exclude acute-on-chronic bronchitics, for whom steroids are known to work), we narrowed this subset to six preferred trials, of which four showed steroids to work. The remaining two trials examined small numbers of patients (12 and 16 respectively), and did not exclude the possibility of type II error (ie, failing to appreciate a steroid effect that was present). Thus, the best available RCTs do suggest that steroids can work, but in none of these six trials was the benefit universal. Even in the study with the greatest fraction of steroid responders, only 56 percent of patients experienced improved airflow with steroids (versus 13 percent of placebo recipients).

Despite the evidence that steroids can be effective in stable COPD, we remain unable to reliably predict steroid responsiveness, so that clinicians must rely on careful steroid trials in individual patients whose COPD remains disabling despite usual treatment. Strategies like the "N of 1" crossover trial, recently advocated by Guyatt et al, may improve these clinical assessments, which should certainly consider the patient's functional capacity and dyspnea, in addition to measurements of airflow. Recent work shows that both of these outcomes can be measured rigorously, and that COPD patients can experience treatment responses that are not measurable by spirometry alone.

Because we know that steroids can work but cannot predict who will respond, we will continue to rely on individual empiric trials until better information becomes available.

James K. Stoller, M.D., F.C.C.P.,
Cleveland

Department of Pulmonary Disease, Cleveland Clinic Foundation.
Reprint requests: Dr. Stoller, Department of Pulmonary Medicine, 9500 Euclid Avenue, Cleveland 44106

References

5 Beerel R, Vance J. Prednisone treatment for stable pulmonary...
Medical Caring for the Smoker
Ethical Responsibility Works Both Ways

In a recent editorial, Timothy Givens has argued forcefully that smokers ought to bear the financial responsibility for the increased cost of health care due to the harmful effects of tobacco use. In proposing a direct tax on tobacco products commensurate with the health care expenses involved, he claims that this move is justified as a method of correcting a "fundamental aberration in American thinking: an increasing reliance on others for our health and well-being."

Multiple problems are raised by this too-easy answer to the question of ethical responsibility, which is a thorny ethical question raising the puzzle of free will/determinism. We have argued that there is a scientific content to medical ethics, and that part of that content involves self-love, self-care, and concern for one's biologic well-being. There is also little doubt that most people engage in self-harmful behavior, and we argue that medical ethics can call that behavior unethical, but that should do so with understanding, compassion, and the humility based on the knowledge that there are very few saints among us. Having said that, we cannot agree with Givens' inference when he quotes us to support his position that since we have an ethical responsibility for our biologic welfare, if we act to violate that welfare we should be economically on our own.

We know it is a conclusion currently in fashion, emphasizing the maxim in principle and zero risk, creating a mythology of individual autonomy and self-reliance, and pursuing cost containment. In medical ethics, people are seriously asking: Why should society pay for genetically ill children whose parents knew a genetic disease was present prenatally and chose to continue the pregnancy in spite of it? Why should society pay for the medical care of lung cancer victims who chose to start smoking and refused to stop? Why should society pay to treat cirrhosis of the liver, esophageal varices, and Korsakoff syndrome in alcoholics who continued to drink? Why should society pay for accident trauma in car passengers who wouldn't wear seat belts? For hypertension in overweight persons who wouldn't diet? For dehydration in anorexics who wouldn't eat? For heart attacks in businessmen who wouldn't slow down—or jog—or quit caffeine—or eat margarine and vegetable oil instead of butter and olive oil—or eat butter and olive oil instead of margarine and vegetable oil? The list could encompass every epidemiologist's nightmare. There is an ethically and scientifically valid affirmative answer to each of these questions, good reasons why society should respond with medical care.

Who Decides Who Will Smoke?

We must reckon with the fact that decisions to smoke and to continue smoking are complex phenomena with many societal, psychologic, and physiologic determinants. Usually initiated during adolescence when susceptibility to peer pressure and mass media advertising is at its peak, when impulsivity is high and the foundations of self-esteem and considered values are unsecured, this initial experimentation rapidly becomes addictive. While not denying smokers' responsibility for their choices, we cannot simplistically stop there. Human choices always take place in a complex, biopsychosocial context which sharply conditions their range and probabilities, and for which the rest of us bear some responsibility. For example, an account of