As is so often the case in medicine, the more cumbersome the diagnostic label the more likely that it is being used to hide our ignorance of its pathogenesis.

References


S. R. MEADOWS
University of Leeds
Department of Paediatrics and Child Health, 27 Blundell Street, Leeds LS1 3ET

Slow-release theophylline preparations

Sir,

This study by McKenzie and Baillie (Archives, 1978, 53, 943) indicates the growing appreciation that theophylline has the potential to control the symptoms of chronic asthma when serum levels are maintained at between 10 and 20 μg/ml. As they suggest, sustained-release theophylline formulations offer therapeutic advantage by allowing more stable serum theophylline concentrations; this results in longer intervals between doses than are possible with either cromoglycate or β-agonist bronchodilators. Not all sustained-release theophylline preparations are completely and reliably absorbed, however, and each product differs in its absorption characteristics even when absorption is complete (Weinberger et al., 1978).

The degree to which a theophylline formulation maintains acceptably stable levels relates to both the rate of absorption of the product and the rate of elimination of the individual. As children have average half-lives of elimination of 3–7 hours, slowly absorbed products are particularly important if excessive fluctuations in serum theophylline concentration are to be avoided. The clinical importance of lessening these fluctuations has been shown by the decrease in bronchodilatation (Levy and Koyosooko, 1975), and blocking of exercise-induced bronchospasm that is parallel to decreasing serum concentration (Pollock et al., 1977). While McKenzie and Baillie argue for the convenience of 12-hour dosing with the sustained-release preparations, their data (McKenzie and Baillie, 1978) and ours (Weinberger et al., 1978) suggest that 8-hour dosing may often be more appropriate except for the slowest of the reliably and completely absorbed sustained-release preparations or for patients with slow rates of elimination.

The rate of elimination of theophylline also determines dosage (Jenne et al., 1976; Ginchansky and Weinberger, 1977). The problems that can result from the variable dosage requirements for theophylline were illustrated in a study that compared theophylline with cromoglycate (Cromolyn, Intal) performed at the Hammersmith Hospital and at two residential treatment centres for asthma in Denver (Hambleton et al., 1977). Whereas all of the patients in Denver tolerated theophylline, 6 patients at the Hammersmith Hospital did not, and therefore could not enter the study. The difference can be attributed to the manner in which theophylline dosage was determined. Each patient in Denver was given an individual theophylline dose while an 'average' dose, similar to that recommended by McKenzie and Baillie, was initiated in all the Hammersmith Hospital patients. The resulting intolerance in some patients was predictable (Wyatt et al., 1978).

We have found that clinical titration using serum theophylline measurement as a guide gives a high degree of safety and provides the greatest likelihood of efficacy in the management of chronic asthma (Ekwo and Weinberger, 1978; Hendeles et al., 1978).

References


MILES WEINBERGER
University of Iowa,
Department of Pediatrics,
Pediatric Allergy and Pulmonary Division,
Iowa City,
Iowa 52242, USA