LETTER TO THE EDITOR

Lung bioavailability of generic and innovator salbutamol MDIs

The statement by Clark et al (March 1996; 51:325–6) that “the coefficient of variation for urinary salbutamol was approximately double that for plasma salbutamol” cannot be made with confidence until the authors have validated the protocol they are using. Hindle and Chrystyn1 reported that the relative bioavailability of salbutamol to the lung could be used to compare two Inhalated products/ inhalation methods by measuring the amount of salbutamol excreted in the urine in the first 30 minutes after inhalation. Their method was to start at time zero, inhale four consecutive doses (with one minute between each dose), and then provide a urine sample at time t = 30 minutes. The protocol used by Clark et al is 12 sequential inhalations over six minutes and then a urine sample is collected for the measurement of salbutamol excretion 30 minutes after completion of the 12 inhalations. Thus, urine is collected over the first 36 minutes compared with 30 minutes for the method of Hindle and Chrystyn. This the authors confirmed during a poster discussion session at the British Thoracic Society’s winter meeting in December 1995. We have been involved with further studies to validate our method so that we can extend our work to the use of nebulisers. At present we have data on five healthy volunteers (four men) who swallowed 100 µg salbutamol solutions at t = 0, 2, 4, 6, and 8 minutes and provided urine samples at 0, 30, 40, and 60 minutes after swallowing the first salbutamol dose. The mean (SD) rate of salbutamol urinary elimination from t = 0–30, 30–40, and 40–60 minutes was 0.08 (0.11), 0.72 (0.76), and 0.99 (0.38) µg/hour, respectively (raw data file). Similar results follow the inhalation of five sequential 100 µg salbutamol inhalations at t = 0, 2, 4, 6, and 8 minutes (that is, each separated by two minutes over six minutes (5-79), 2-4-6 (5-79), 17-60 (6-69) µg/hour, respectively. Thus, interference from the salbutamol delivered to the body by the oral route would be present in the urine samples collected between 30 and 40 minutes after the first Inhalated dose. This suggests that the urine samples collected by Clark et al over the first 36 minutes after the start of the first inhalation would include salbutamol absorbed by the oral route. The presence of drug from oral absorption could account for some of the greater variability of their results compared with the reported plasma salbutamol concentrations. Clark et al claim that the maximum plasma concentration, Cmax, after inhalation may be used as a direct measure of absolute drug bioavailability. However, the measurement of Cmax is an indirect method of bioavailability since it measures salbutamol concentrations in plasma rather than amounts in the lung. Furthermore, the authors do not present supporting data following oral administration to the 10 healthy men they studied. The absence of intravenous data or direct in vivo information into the lungs with their method means that it compares relative lung bioavailability, not absolute.

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BOOK NOTICE


This book represents a successful attempt to incorporate in a practical way the huge amount of information published regarding HIV and AIDS since the first edition in 1989. If anything, the term “pocket book” may underestimate the quantity of information which is concisely expressed on every aspect of HIV disease.

There are 18 chapters each by different authors with practical experience in their topic, although the editors have maintained throughout a uniform style of presentation which is thoroughly readable. Chapters on epidemiology and natural history and international aspects of HIV/AIDS outline the global spread of the disease and the important regional differences in natural history. Each chapter on the main organ systems initially provides a helpful differential diagnosis of common presenting symptoms (including some diagnosis for HIV), then reviews the important conditions in more detail. These reviews are authoritative and well balanced between giving the practice of the author and providing an overview of current literature. The chapter on therapeutic guidelines comprehensively presents treatment regimes for the major opportunistic infections, including drug side effects and drug interactions. Chapters on HIV in pregnancy, paediatrics, and in relation to blood products and intravenous drug misuse provide updated information of great use to counselling patients. Moreover, there is a chapter providing practical guidelines for counselling HIV patients in general. Especially useful and thoroughly presented is the chapter on aspects of palliative and terminal care.

The book has an index and each chapter is referenced. There are a limited number of black and white illustrations.

This excellent book is particularly recommended to medical students, junior hospital doctors including MRCP students, and general practitioners in high prevalence areas. Chest physicians will find this book useful not only for information on the respiratory manifestations, but also on the diseases of other organ systems likely to coexist in their patients infected with HIV. – DF

NOTICE

European Asthma School

A three-day intensive course on Experimental and Clinical Aspects of Asthma will be held in Ghent, Belgium on 19–21 November 1996. For further information please contact the Department of Respiratory Diseases, University Hospital, De Pintelaan 185, B 9000 Ghent, Belgium. Phone: 32 9 2402011. Fax 32 9 2402341.
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