Audit of serum theophylline concentrations in patients from general practice

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SUMMARY. From the repeat prescription register of a British general practice, 37 patients regularly taking theophylline preparations were identified. Measurement of their serum theophylline concentration showed that less than 25% of these patients were achieving a theophylline concentration in the therapeutic range. Reasons for this are discussed.

Introduction

THEOPHYLLINES have been increasingly widely used in recent years in asthma and chronic bronchitis, both here and in the USA, and prescribed widely by both general practitioners and hospital doctors.[1-3] It is generally accepted that for effective bronchodilation a serum theophylline level between 55 and 110 μM must be achieved.[1] Despite this knowledge, audits of levels actually achieved in two hospital-based populations of patients taking this class of drugs showed that levels in the therapeutic range were only achieved in 43%[4] and 37–47%[5] of patients. It is accepted[1] that general practitioners tend to underdose patients on these preparations for fear of the toxic effects associated with overdose; the implication of this is that few patients get effective bronchodilation from the use of this difficult group of drugs.

An audit of theophylline use in a British general practice has therefore been carried out.

Method

Patients regularly taking theophylline or a theophylline derivative were identified from the repeat prescription register of a 12-partner practice caring for 33 000 patients. Patients identified were then contacted by telephone and asked to take part in the study. Patients not on the telephone were visited and those not at home were left a letter asking them to contact the practice. Patients excluded from the audit were those under 16 years of age, those unable to give informed consent and those who had received intramuscular or intravenous theophylline or who had otherwise altered their regimens within 36 hours. Permission was also obtained from each patient's general practitioner and the area ethical committee.

After informed verbal consent was obtained, a blood sample was taken from eligible patients two to four hours after they had taken their regular theophylline medication. Blood sample analysis was carried out by the Regional Clinical Pharmacology Department using a Cyva emit assay. Information was also recorded about age, other drugs, and the patient's disease.

Results

Thirty-seven patients on the repeat prescription register were regularly taking theophylline preparations and were over 16 years of age, a mean of 3.1 patients per general practitioner. Eighteen were between 16–25 years of age and 19 were between 65–90 years of age. Most patients (23, 62%) were being treated for asthma, nine for chronic bronchitis, three for other reasons and for two patients the reason for prescribing theophylline was not known. Phyllocontin Continus (Napp), the sustained-release aminophylline (theophylline ethylenediamine) preparation, was by far the most widely prescribed drug; 34 of the 37 patients were taking it. Drugs and dosages are plotted against serum theophylline levels in Figure 1.

Twenty-eight patients (75%) had a serum theophylline concentration below the therapeutic range. None had a serum concentration greater than the therapeutic range. Three patients were taking regular nocturnal medications only; three hours after their usual dose none of these patients had serum theophylline concentrations in the therapeutic range.

Discussion

This survey of patients regularly taking theophylline preparations has shown that less than 25% of patients on regular theophylline medication achieve serum theophylline concentrations in the therapeutic range of 55–110 μM and that no patients had concentrations above the therapeutic range. Thus at least three-quarters of these patients may not be receiving optimal benefit from these drugs.

There are no figures available to allow a direct comparison of results from this practice with other practices. However, the use of these compounds probably does not vary greatly between practices. The particular product prescribed is likely to make little difference to the achieved theophylline concentration since the oral dose of theophylline is only loosely related to serum

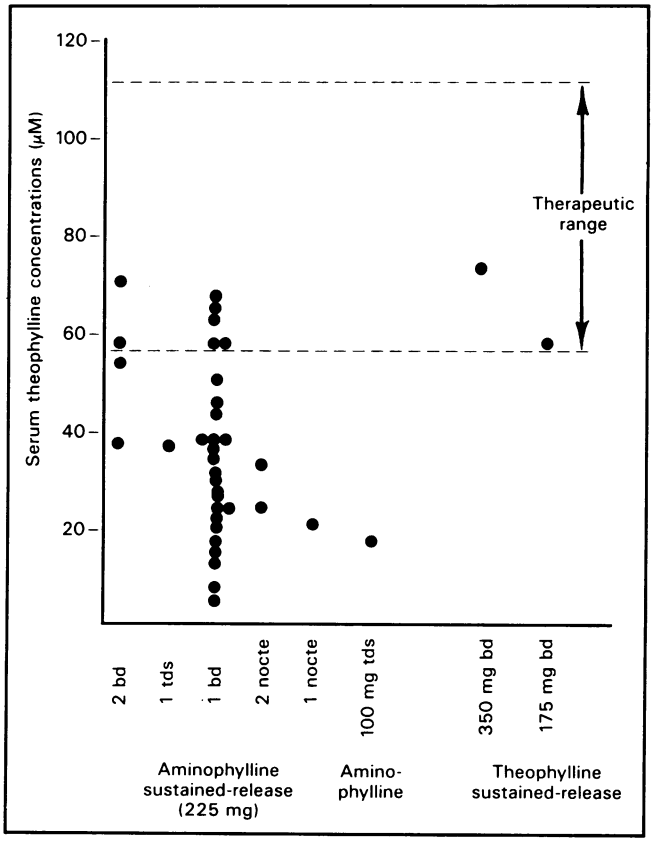

Figure 1. *Scattergram to show distribution of serum theophylline levels versus drug type and dose for 37 patients.*

concentrations.[4] All the patients in this survey were taking standard doses. General practitioners rarely perform serum theophylline assays (personal communication, Clinical Pharmacology Department, Glenfield General Hospital). Lastly, the average number of prescriptions for theophylline per practitioner in 1982 in England was 24 (personal communication, Prescription Pricing Authority). This seems compatible with this survey which demonstrates an average of three regular theophylline users per practitioner.

It is likely that the results of this survey are typical of most general practitioners' use of theophyllines. What factors could contribute to the low serum levels reported? Patients who admitted that they had not complied with their therapy were excluded. Blood samples were taken at a time when serum theophylline concentrations would have been highest; for Phyllocontin (aminophylline, Napp) and Theo-Dur (theophylline, Fisons) in regular users peak concentrations occur at three to four hours after the dose.[6] The most likely reason for the low theophylline levels is failure to ensure an adequate oral dose of theophylline. Where alteration in theophylline by concurrent drug therapy or illness[4] is suspected it is even more important to titrate the oral dose against serum theophylline concentration.

It is possible to determine an initial oral dose of theophylline that will produce a therapeutic serum concentration by using a nomogram.[7] Subsequently, to achieve therapeutic levels serum theophylline concentrations must be measured. Wider appreciation of the difficulties surrounding the use of these drugs should increase the number of patients deriving full benefit from their prescription. Currently, it is doubtful how much benefit patients receive from the use of theophylline-containing drugs.

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