

Theophylline Usage in Patients with Acute Asthma Presenting to a Central Hospital

P MUTANDWA, P NEILL

SUMMARY

A survey was conducted to investigate the medication taken by asthmatics presenting to a casualty department, particularly with reference to theophylline. Serum levels of theophylline were measured to give an indication of the effectiveness of the therapy. Most patients were found to be taking some form of theophylline regularly, and serum levels measured were in the therapeutic range. Under-dosing with theophylline does not appear to be a factor in the failure to prevent asthmatic attacks in these patients.

*Department of Clinical Pharmacology,
Godfrey Huggins School of Medicine,
University of Zimbabwe.*

INTRODUCTION

In Zimbabwe the cheapest and most easily available form of asthma therapy is some form of theophylline, usually compounded with ephedrine. Theophylline is a useful bronchodilator but there is a degree of inter-individual response.¹ It has been found that the effectiveness of the drug (and also its toxicity) is related to serum levels of theophylline,² a bronchodilator effect is measurable above 5 µg/ml and this effect increases towards 20 µg/ml. However, above 15 µg/ml side effects, initially gastrointestinal, may become noticeable. Consequently, the optimum level lies between 10 and 15 µg/ml.

We wished to assess the usage of theophylline compounds by asthmatic patients presenting to casualty, and by measuring theophylline levels, assess whether sub-optimal treatment was part of their reason for presentation.

METHOD

Twenty-six patients presenting to casualty at Parirenyatwa Central Hospital had a diagnosis of asthma made on the following criteria:

1. A past history of recurrent dyspnoea and diagnosis of asthma
2. No history of cigarette consumption
3. Presence of wheeze in the chest on examination, with no other cause for the wheeze.

A questionnaire was administered to these 26 patients. Ten ml of serum was taken from each of these patients on presentation to casualty, before any further medication was given. The specimens were spun down and the separated serum stored at 4 °C before analysis of theophylline levels. The levels were measured by an enzyme-linked method on an EMIT CP 5000. Nine of the specimens were considered unsuitable for analysis due to haemolysis which occurred in the centrifuging process. Consequently 17 of the specimens were suitable for analysis.

RESULTS

1. Results of questionnaire

i) *Medication taken within 24 hours prior to presentation to casualty:* Twenty patients had taken some form of theophylline/ephedrine

compound tablet. Of these 20 patients, 3 had been to a primary care clinic and received aminophylline either intravenously (2) or as a suppository (1). Five of these 20 had also used a salbutamol inhaler. Two patients had taken aminophylline tablets. One patient used a salbutamol inhaler alone. Three had taken no medication.

ii) *Medication taken regularly in the month prior to admission:* Eighteen patients of the 26 were taking medication on a daily basis. All of these 18 were taking theophylline/ephedrine compound tablets which contain 130 mg theophylline per tablet. Sixteen patients were taking a dose of 2 tablets three times a day. Two were taking 1 tablet three times a day. Five of the patients were using salbutamol inhalers on an 'as needed' basis. Two of these 5 patients were also on regular daily prednisolone.

iii) *Admission for asthma in the previous year:* Twelve of the 26 patients had one or more previous admissions in the foregoing year.

2. Serum theophylline levels

Seventeen patients had levels measured. One patient had a level of 3,7 µg/ml, a sub-therapeutic level. This patient was not one of the patients taking medication on a regular basis. One patient had a level of 26,8 µg/ml, a level which may cause toxicity. This patient was one of those who had received an intravenous injection of aminophylline at his primary care clinic. The other 15 patients had levels ranging from 9,5 – 19,1 µg/ml. Of these 17 patients, 16 took theophylline on a regular basis. All the 17 patients had taken theophylline in the previous 14 hours.

Time range between presentation to casualty and taking the last dose of medicine before presentation was 5–14 hours. In nine patients the serum theophylline levels were not measurable for technical reasons. Of these nine patients, four of them were not taking theophylline in any form, hence no theophylline would be expected to be found in their serum. Of the remaining five, there was no obvious factor that would suggest that their theophylline levels should be markedly different to those patients whose levels

were measured. There was no excessive delay in centrifuging their specimens; their time of presentation to casualty was not different from that of the measured group; there was no evidence of clinical haemolysis, i.e. the haemolysis which prevented measurement of the theophylline was caused by collection technique.

DISCUSSION

Of 26 patients diagnosed as presenting with an asthmatic attack, 22 (88%) had taken theophylline in some form in the previous 24 hours. For 17 (65%) of these patients theophylline was the only medication they had taken. Theophylline, therefore, constitutes an important component of asthma therapy in a Zimbabwean context. Theophylline is accepted as an effective bronchodilator.² Its effectiveness is, however, related to its serum levels.¹ It might be that failure to establish adequate levels is part of the reason for the theophylline therapy of these patients not preventing them presenting to casualty.

However, in 16 of the 17 patients whose serum theophylline levels were measured, adequate levels were present. Hence it appears that the medication the patients received achieved its purpose as far as adequate dosage is concerned.

What explanations then may be offered for the theophylline not having achieved its task of preventing an asthmatic attack in those patients taking theophylline (or theophylline/ephedrine) alone? The obvious answer is that the state of the asthma in these patients was such that it was too severe to be solely controlled by theophylline. As witness to this is the fact that 12 of the total 26 patients had already been admitted with an asthmatic attack, once or more often in the previous year.

There are, however, two other factors that may be considered. Firstly, all of the patients were Zimbabwean Blacks. This population has never been studied in terms of bronchodilator effectiveness of theophylline. Clinical experience indicates, however, that theophylline is effective. A simple study would clarify the situation, but it is unlikely that this is important. Secondly, theophylline levels were measured when the patients presented to casualty. It may be that at the

time of the onset of the attack serum levels are too low to prevent the attack. However, 16 of the 17 patients whose levels were measured were taking theophylline on a regular basis, and it is likely, accepting that there are peaks and troughs in serum levels, that these patients had adequate levels at the time of the onset of the attack.

It may be noted that the majority of the patients were taking a theophylline/ephedrine compound preparation. Though ephedrine has some bronchodilator effect alone,⁴ the addition of ephedrine to theophylline being taken in optimal doses adds nothing or only small increments of bronchodilation^{3,4} and may increase side effects.⁴ Hence the presence of the ephedrine should not influence the effectiveness of the medication being taken.

We can conclude that the majority of patients presenting with an asthmatic attack to a central hospital in the Zimbabwean context are taking theophylline in some form and that the amount they are taking is adequate to achieve therapeutic levels. This group of patients needs additional therapy to prevent their presentation with acute asthma.

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