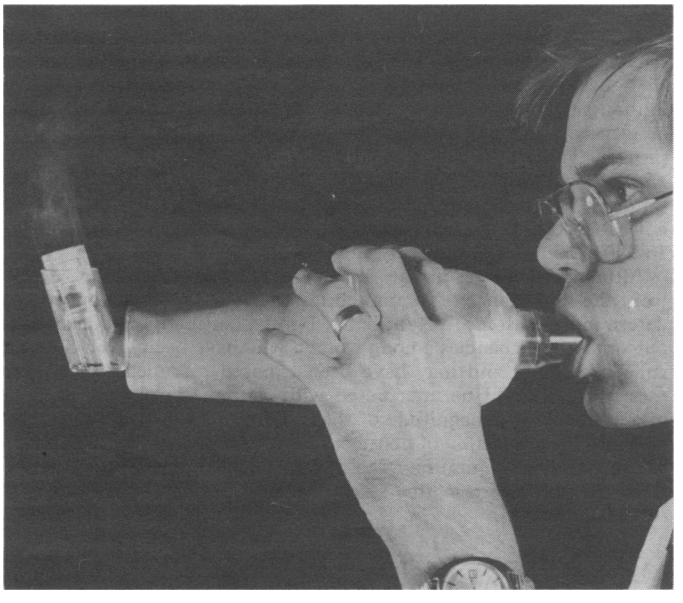
Potential limitations of a conical spacer device in severe asthma

A conical spacer device (Nebuhaler, Astra) has been suggested as an alternative to a nebuliser for the delivery of bronchodilators in acute severe asthma[1] and chronic stable asthma.[2] When using the conical spacer coordination of inspiration with actuation of the metered dose aerosol is unnecessary as a one way valve closes on expiration, allowing aerosol in the 750 ml reservoir to be inhaled over several breaths.

We describe a patient who failed to obtain relief from her terbutaline aerosol used through the conical spacer when her expiratory flow became too low to close the one way valve, thus allowing expired air to blow the aerosol out of the reservoir. We measured the flow rates necessary to close the valves on 10 conical spacers and examined the implications of our findings.

Patient, method, and results

A 35 year old woman with unstable asthma had been prescribed a conical spacer device to use with her terbutaline inhaler. Initially she obtained good symptomatic relief of her wheezing whenever she used the device. After several weeks her asthma deteriorated with severe morning wheeze which was unrelieved by terbutaline through the conical spacer. At these times her expiratory flow rates were too low to close the spacer valve and she therefore exhaled through the reservoir of the device (see figure). Terbutaline taken from the metered dose aerosol in the conventional manner, however, relieved her wheeze. When her wheezing was less severe she found that she could close the one way valve on the spacer and that again it gave symptomatic relief.



Simulation with solid CO_2 of subject with low flow rate failing to close valve on expiration and blowing aerosol out of reservoir.

We examined the spacer and found that it was clean and working normally. We measured the flow rate of air that was necessary to close the valve on 10 separate manoeuvres in three positions—horizontal, at 45° upwards, and at 45° downwards—using a Morgan differentiating dry spirometer. We studied the patient's conical spacer and nine other identical devices.

When held horizontally, as illustrated by the manufacturers, a mean flow rate of 68 l/min (range 44-94) was needed to cause valve closure. When held upwards at 45° a considerable increase in the flow rate was necessary to close the valve (mean 83 l/min; range 67-94). Conversely, when pointed downwards at 45° nine of the 10 valves closed at zero flow.

Comment

A theoretical advantage of the conical spacer is that it provides a reservoir of aerosol that can be inhaled over several breaths through a one way valve. It is useful in asthmatics with low peak flow rates and small vital capacities who require several breaths from the reservoir to obtain maximum benefit. The one way valve must close to prevent patients breathing out through the reservoir and wasting the aerosol, as this case illustrates.

There are no published data on the flow rates required to close the spacer valves. Our findings suggest that peak flow rates present in severe asthmatic attacks may fail to close these valves, thus causing wastage of the aerosol. Undue reliance on the device in these circumstances might have serious consequences. To some extent this may be overcome by pointing the device downwards, allowing gravity to close the valve. The inability of a patient to close the valve on the spacer device, while being an indication of the severity of the asthmatic attack, may limit the clinical benefit that can be obtained from the conical spacer in severe asthma.

[1] Morgan MDL, Singh BV, Frame MH. Terbutaline aerosol given through pear spacer in acute severe asthma. *Br Med J* 1982;**285**:849-50.
[2] O'Reilly JF, Buchanan DR, Sudlow MF. Pressurised aerosol with conical spacer is an effective alternative to nebuliser in chronic stable asthma. *Br Med J* 1983;**286**:1548.

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Renal proximal dysfunction in patients with rheumatic diseases

Although glomerular proteinuria is uncommon in early rheumatic diseases, it is a complication of advanced disease caused by the direct effects of the disease on the kidney or the action of nephrotoxic drugs, or both.[1 2] Alterations in proximal tubular function may be a sensitive index of the reaction of the kidney to various toxic stimuli.[3] This form of tubular dysfunction, which is shown by increasing amounts of protein of low molecular weight in the urine, cannot generally be detected by routine urine analysis. We report a study of proximal tubular function in 87 consecutive patients with severe arthritis admitted to a regional rheumatic disease centre.

Patients, methods, and results

A 10 ml random sample of urine was collected from 87 patients (34 men, 53 women), of whom 43 had rheumatoid arthritis, 17 osteoarthrosis, nine ankylosing spondylitis, six seronegative polyarthritis, and 12 other diseases. The urine specimens were collected soon after admission, usually before the disease had been brought under control with drug treatment or physiotherapy. They were collected in the morning but not at a fixed time in relation to drug treatment as the patients were receiving a wide variety of drugs.

Urine samples were preserved with a thymol crystal and tested routinely with Albustix. In addition, the pH was measured, and concentrations of albumin, α_1 microglobulin, and β_2 microglobulin were measured by single radial immunodiffusion using specific antisera and standards obtained from Behringwerke, Marburg, Germany (α_1 microglobulin and albumin) and Dakopatts, Copenhagen (β_2 microglobulin). All protein measurements were corrected for urinary creatinine concentration and expressed as mg/g creatinine. Total urine protein concentrations were measured by nephelometry using the trichloroacetic acid microprecipitation method recommended for the measurement of total protein in cerebrospinal fluid (Hyland Laser nephelometer instrument application sheet).

Albustix testing showed that 24 of the 87 samples contained a trace of protein, seven showed 0·3 g/l, two showed 1·0 g/l, one showed 3 g/l, and the remainder gave negative results. The upper limit of normal urine α_1 microglobulin concentrations is 10 mg/l creatinine (mean (SD) 3 (2·5) mg/g); 30 of the 87 patients had concentrations higher than this (mean 33 (24) mg/g) creatinine (range 10-125 mg/g). Urine β_2 microglobulin concentrations were raised in 12 patients (>10 mg/g creatinine in eight); the upper limit of normal concentrations is 0·1 ng/g creatinine, which is too low for detection by radial immunodiffusion. Raised urine albumin concentrations (>50 mg/g creatinine) were found in 15 patients, in five of whom albumin was the only protein at an abnormal concentration. Of the 35 patients who showed evidence of either proximal tubular dysfunction or increased urinary albumin excretion, only 18 had raised total protein concentrations (>150 mg/g creatinine) as measured by nephelometry.

Of the 21 patients with the most pronounced tubular dysfunction as shown by impaired reabsorption of low molecular weight proteins, whose mean