Clin. Otolaryngol. 1987, **12**, 7–10

The effect of Mucodyne on nasal clearance in healthy adults

G. J. C. SMELT, S. W. LEE, J. G. HARDY AND C. G. WILSON

Department of Otolaryngology, Department of Medical Physics and Department of Physiology and Pharmacology, University Hospital, Queen's Medical Centre, Nottingham

Accepted for publication 16 June 1986

SMELT G. J. C., LEE S. W., HARDY J. G. & WILSON C. G. (1987) *Clin. Otolaryngol.* **12**, 7–10

The effect of Mucodyne on nasal clearance in healthy adults

A randomized double-blind cross-over trial in healthy young adults compared the effect of S-carboxymethylcysteine (2.25 g per day for 7 days) against placebo on nasal mucociliary clearance. The clearance rate of a radio-labelled aqueous test spray was measured by gamma scintigraphy. Analysis of the data revealed no significant effect of the drug compared to placebo.

Keywords *S-carboxymethylcysteine nasal mucociliary clearance gamma scintigraphy*

'Mucodyne' and its recent competitor 'Mucolex' are registered trademarks for preparations whose active ingredient, S-carboxymethylcysteine, is an analogue of cysteine. Cysteine is a non-essential sulphur containing amino acid that is utilized in the formation of taurine. This in turn combines with cholic acid to form the bile acid, taurocholic acid. The free thiol group which reduces the disulphide bond in mucus, is protected by a methyl group to prevent gastrointestinal irritation.[1]

The general fate of sulphur-containing amino acids is catabolism in the liver, however most of S-carboxymethylcysteine is excreted unchanged within 30 min via the kidneys.[2] Following Mucodyne ingestion the transient increase in S-carboxymethylcysteine in the blood stream is widely accepted as having a beneficial effect in a number of clinical conditions, most of which involve defective mucus and mucociliary transport as common pathogenic features. There have been several studies suggesting improvement in glue ear,[3] chronic sinusitis,[4] chronic bronchitis and bronchiectasis.[5] Although there is no consensus on the mode of action of the modified amino acid, it is generally believed that either the viscosity of the mucus decreases or a 'fluidification of sputum' develops.[6]

Many experiments have been carried out *in vitro*,[7] with animals and with patients[5, 6, 7] but few studies have been undertaken in normal subjects to examine the effect on mucus transport *per se*. The present study investigates the effect of therapeutic doses of Mucodyne on nasal mucus clearance in healthy young adults.

Materials and methods

MATERIALS

The nasal spray comprised an aqueous solution of 0.005% w/v thiomersal and

Correspondence: Dr G. J. C. Smelt, Department of Otolaryngology, Queen's Medical Centre, Nottingham NG7 2UH.

2.0% propylene glycol and was radio-labelled with (^{99m}Tc-labelled) human serum albumin (^{99m}Tc HSA). The ^{99m}Tc HSA was prepared by the addition of 1GBq^{99m}Tc-sodium pertechnetate in 1 ml 0.9% sodium chloride solution, to a vial containing 10 mg HSA (kit for labelling human albumin with technetium-99m(TCK-2): CIS (UK) Limited, London). To 5 ml of the unlabelled preparation was added 0.1 ml ^{99}Tc^{m}-HSA solution. The solution was administered from a Mistette Mark II nasal spray application (Calmer-Albert GmbH, Reigate) having a nominal ejection volume of 100 μl and a spray cone angle of 60 degrees.

SUBJECTS

Following DHSS and local ethical committe approval, 3 scintigraphic studies were undertaken a week apart in a randomized, double-blind, cross-over trial (see Table I). The effect of taking 750 mg Mucodyne 8-hourly for 7 days, was compared to that of placebo in 3 male and 3 female healthy volunteers aged 20–22 years.

METHODS

The deposition and subsequent clearance of the solution were monitored by gamma scintigraphy, as previously described.[9] The gamma camera had a 40 cm diameter field of view and was fitted with a low energy (160 keV maximum) parallel hole collimator. The camera was tuned to detect the 140 keV radiation of technetium-99m with a 20% energy window. The insufflator was filled with 5 ml radio-labelled solution and primed by activating the pump 15 times into a closed system. With the subject in an upright posture, the applicator nozzle was positioned parallel to the dorsal ridge with the tip 3–5 mm into either nostril. A single dose was dispensed during normal inhalation with the contralateral nostril open. The average volume ejected from the primed pump was 72 μl (s.d. = 9 μl), radio-labelled with 1–2 MBq technetium -99m.

Lateral views of the head, each of 1 min duration, were recorded immediately after insufflation and at frequent intervals over a 90-min period. The nostril containing the tracer was placed nearest the collimator, and a perspex rod attached to the collimator was used to ensure accurate repositioning. The images were recorded by computer for subsequent quantification. Using the computer, regions of interest were defined around the image of the whole nasal cavity. The deposition site in each view was displayed on a television monitor. The count rates from each region were corrected for background counts and for radioactive decay, and expressed as a proportion of the count rate from the whole nasal cavity immediately following administration. The relative humidity in the imaging room was $45 \pm 7\%$ throughout the study.

Results

The proportion of labelled nasal spray remaining in the nasal cavity 30 min after insufflation was very nearly the same in the 2 groups tested: those after 1 week of placebo and those after 1 week of Mucodyne (Table 1). Total clearance times

Table 1. Proportion of nasal spray cleared 30 min after application

	Proportion remaining in nasal cavity (%)			
Subject	*Before placebo*	*After placebo*	*Before Mucodyne*	*After Mucodyne*
1	64	89	40	78
2	50	64	75	46
3	19	41	83	68
4	59	37	47	42
5	87	26	28	43
Mean ($\pm$s.d.)	56 (24)	51 (26)	55 (23)	55 (17)

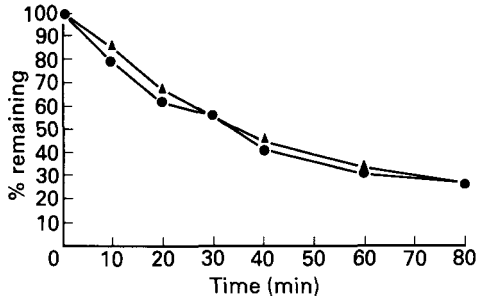

Figure 1. Clearance of spray from the nasal cavity before (●) and after (▲) 1 week of treatment with Mucodyne.

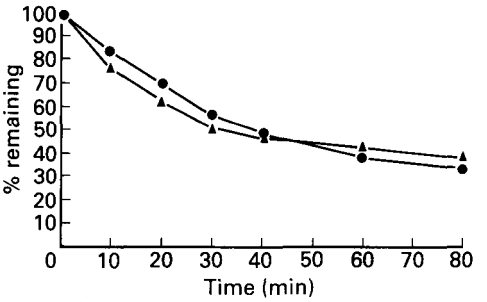

Figure 2. Clearance of spray from the nasal cavity before (●) and after (▲) 1 week of treatment with placebo.

of the spray from the nasal cavities of the same 2 groups were also very similar (Figures 1 and 2).

Discussion

S-carboxmethylcysteine is a widely prescribed drug. At University Hospital, Nottingham and its associated hospitals an average of 8.1 l of Mucodyne was dispensed monthly during 1984 with Mucolex adding 0.5 l per month. This represents about 6 adult monthly courses or 10 such recommended courses for children. The specialties that may be expected to prescribe the drug (ENT, general medicine and paediatrics) see approximately 5000 patients a month. This does not appear to be a high prescription rate and may reflect a relative reluctance of specialists to prescribe this preparation. In 1985 S-carboxymethylcysteine was not included in the list of drugs approved for National Health Service prescription.

The efficacy of S-carboxmethylcysteine has been questioned in some studies[9] and supported in others[6] but even those convinced of its beneficial therapeutic effects find it difficult to explain its mode of action. If Mucodyne is effective, the present study has found no evidence for it working by altering nasal clearance in normal subjects.

Nasal clearance is a measurement that depends on mucus quality and quantity as well as the actions of the ciliated epithelium. It might be expected, therefore, to reflect the sort of changes S-carbocysteine is thought to make in diseased respiratory epithelium, including that of the middle ear cleft. Nasal clearance may also be a good indicator of the effectiveness of the 'respiratory mucosa' of the pharyngotympanic tube.

Thomson[10] was criticized by Edwards[6] for not giving Mucodyne for longer than 4–7 days in his study negating its use in bronchitis even though all the positive effects demonstrated in Edwards' study occurred after only 6 or 7 days treatment. It may be that Mucodyne has no effect on normal physiology but can affect pathology. The increased clearance found by Sakakura[4] in chronic sinusitis using the saccharin method after a month of Mucodyne may also depend on the presence of pathology. At a Royal Society of Medicine forum[5] it was speculated that the modified amino acid may be an anti-inflammatory agent or that it may prevent hyperplasia of goblet cells. Bronchitics have a relative preponderance of goblet cells in their smaller airways and this may be why a course of S-carboxymethylcysteine might cause 'fluidification of sputum' in these patients.

Acknowledgements

We wish to thank Berk Pharmaceuticals Ltd for the supply of active and placebo

Mucodyne capsules and Miss S. P. Dodds for typing the manuscript.

References

1 BROWN D.T., POTSIC W.P., MARSH R.R. & LITT M. (1985) Drugs affecting clearance of middle ear secretions: a perspective for the management of otitis media with effusion. *Ann. Otol. Rhinol. Laryngol.* **Suppl. 117, 94,** 3–15

2 WARING R.H. (1980) Variation in human metabolism of S-carboxymethylcysteine. *I.R.C.S. Medical Science* **8,** 264–265

3 KHAN J.A. (1983) Experimental and clinical studies in otitis media with effusion. The role of carbocysteine, *J. Laryngol. Otol.* **Suppl. 97,** 19–21

4 SAKAKURA Y., MAJIMA Y., SAIDA S., UKAI K. & MIYOSHI Y. (1985) Reversibility of reduced mucociliary clearance in chronic sinusitis. *Clin. Otolaryngol.* **10,** 79–83

5 WOOD C. & RUE Y. (Eds) (1982) Mucoregulation in respiratory tract disorders. *The Royal Society of Medicine Forum Series* **5,** 1–28

6 EDWARDS G.F., STEEL A.E., SCOTT J.K. & JORDAN J.W. (1976) S-carboxymethylcysteine in the fluidification of sputum and treatment of chronic airway obstruction. *Chest* **70,** 506–513

7 LIEBERMAN J. (1968) Measurement of sputum viscosity in a cone-plate viscometer: 2. an evaluation of mucolytic agents in vitro. *Am. Rev. Resp. Dis.* **97,** 662–672

8 HUYEN V.N., GARCET S. & LAKAH L. (1966) Experimental hypersecretion of the bronchial mucus of the rat: the study of a mucolytic agent—S-carboxymethyl-cysteine. *Proc. Soc. Biol.* **160,** 1849–1851

9 LEE S.W., HARDY J.G., WILSON C.G. & SMELT G.J.C. (1984) Nasal sprays and polyps. *Nuc. Med. Commun.* **5,** 697–703

10 THOMSON M.L., PAVIA D., JONES C.J. & MCQUISTON T.A.C. (1975) No demonstrable effect of S-carboxymethylcysteine on clearance of secretions from the human lung. *Thorax* **30,** 669–673