

Short Communication

Measurement of Nasal Mucociliary Clearance

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Abstract

Mucociliary transport in the nose serves as the first host defense against the inhalation of atmospheric particulate matter. Nasal Mucociliary Clearance (NMC) is determined to obtain an in vivo measurement of the effectiveness of the interaction between the cilia and mucus. Various techniques are employed for measuring NMC namely saccharin test and tests using dyes or radio labeled particles. Saccharin test is an inexpensive, simple and non-invasive method while methods using radio labeled particles are time consuming, cumbersome and expensive.

ABBREVIATIONS

MCC: Mucociliary Clearance; NMC: Nasal Mucociliary Clearance; NMTR: Nasal Mucociliary Transport Rate; MAA: Macro Aggregated Albumin.

INTRODUCTION

Mucociliary clearance (MCC), a vital key defense mechanism is especially important in the upper airways and sinuses, as it protects the body against noxious inhaled materials [1]. The removal of debris-laden mucus in the sinuses completely depends on MCC, whereas in the lower airways, MCC can be compensated for by other mechanisms like coughing [2]. The nasal mucociliary clearance (NMC) system functions to transport the mucous layer lining the nasal epithelium towards the naso pharynx by ciliary beating in a metachronous fashion at a frequency of 7-16 Hz at body temperature [3, 4]. NMC depends upon two principal components - physiochemical qualities & quantities of mucus and the properties of cilia that propel it (beat frequency & coordination) [5].

NMC is generally determined to obtain an in vivo measurement of the effectiveness of interaction between cilia and mucus [6]. Evidences state that MCC occurs in trachea and main bronchi at a similar rate as in the nose. Thus, NMC is considered to be representative of pulmonary clearance [6].

James et al in their study have reported that the normal NMC time is determined to be up to 20 minutes. Duration of 30 minutes is considered as the cutoff point that discriminates normal subjects from subjects with impaired NMC [7, 5]. (Table 1) Prolonged duration of NMC has been reported in subjects with septal deviations and upper respiratory infections [8]. Drugs like antihistaminics, anti-depressants, adrenaline, acetyl choline and corticosteroids have been reported to influence NMC [8].

Though several approaches serve to determine NMC, there are basically two principles based on which NMC can be determined.

Measurement of the transport of markers placed on the mucosa

- Mucociliary transit time with saccharin –Saccharin test
- Mucus flow rate with
 - 99m Tc-labelled particles–Rhinoscintigraphy
 - 99m Tc-labelled resin particle
- Mucus flow rate with radiopaque Teflon dics
- Mucociliary transit time with colouring substances
- Mucociliary transit time with a combination of dye and saccharin

Measurement of total nasal clearance of a deposited dose

- Gamma scintigraphy (Total clearance of 99m Tc-labelled solutions). [1]

Following is a brief overview on the various methods of measurement of NMC, their advantages and disadvantages.

METHODS OF MEASUREMENT OF NMC

Mucociliary transit time with saccharin –saccharin test

Saccharin test was described by Anderson et al in 1974

Table 1: Duration of Nasal Mucociliary Clearance (NMC).

Normal	Up to 20 minutes
Prolonged	21 to 30 minutes
Severely Prolonged	31 to 60 minutes
Grossly Prolonged	Over 60 minutes



Figure 1 Saccharin test being performed on a subject. The tip of the forceps holds the saccharin particle.



Figure 2 Saccharin test being performed on a subject. Saccharin particle is placed in the medial surface of the inferior nasal turbinate (1 mm behind the anterior end).

and later modified by Rutland & Cole. It is considered to be the standard technique for measurement of NMC.

Prior to the start of the procedure, the subject should spend an hour in a stable environment which is devoid of dust and breeze with relative humidity. A saccharin particle measuring 1mm in diameter is to be placed under direct vision, on the medial surface of the inferior nasal turbinate, at least 1mm behind the anterior end of the turbinate. The position of the subject should be such that the head is flexed 10 degrees. The subject is instructed not to sniff, sneeze, cough, smoke, eat or drink during the test. Subjects are asked to report the taste as soon as it is noted. Subjects with severe watery rhinorrhoea and obstructed nostrils should be excluded. The time from the placement of the saccharin particle to the initial perception of the sweet taste is recorded in minutes. The test is terminated after 60 minutes. If taste is not appreciated after 60 minutes, the test should be stopped and the ability of the subject to taste saccharin directly on the tongue is verified. The test can be repeated in the same nostril on the following day to assess its reproducibility.

Saccharin test is a useful screening technique. It is inexpensive, readily available, non-invasive and simple to perform. The results obtained using saccharin test is similar to those obtained using radio actively labeled particles [6]. Thus, saccharin test has a good coefficient of reproducibility in individuals on different occasions [9]. Saccharin test can be used for serial measurements during treatment, although it should be repeated only after the

sweet taste has completely disappeared (usually after 4 hours). Saccharin test is usually performed prior to referring patients for ciliary beat frequency estimation, as it is found that all patients with primary ciliary dyskinesia have NMC >60 minutes, if correct precautions are observed. The only disadvantage of this method is that the determination of transit time may be influenced by the taste threshold of the patient [1].

Rhinoscintigraphy

Mucus flow rate with 99m Tc-labelled macroaggregated albumin particles: The measurement of mucociliary transport velocity by rhinoscintigraphy with 99m Tc- labeled macroaggregated albumin (99mTc-MAA) is a reliable measure of MCC [10, 11]. Quantitative analyses of nasal mucociliary transport rate (NMTR) can be precisely done with the data generated by Rhinoscintigraphy [12]. Further, Tc-99m-macroaggregated albumin (MAA) is widely used for rhinoscintigraphy in the context of research [10]. Many studies have reported that rhinoscintigraphy is an objective and sensitive method used in the follow-up of nasal and paranasal surgery and for the evaluation of effectiveness of pharmacological interventions in various nasal pathologies. [10, 13-17]

PROCEDURE

Rhinoscintigraphy is performed by administering one droplet (~100 μ Ci that gives about 50 μ Sv radiation dose to the patients) of 99mTc-macroaggregated albumin (99mTc-MAA) (particle size: 10-150 μ m) on the right side, at the base of the nasal meatus and the anterior end of the inferior turbinate using a 27 G syringe. The scintigraphic procedure will result in negligible gamma radiation exposure due to the small dosage of 99mTc-MAA applied. Room temperature is stabilized at 21°C. Images are obtained using a GE-millennium gamma camera system (GE Medical Systems, Milwaukee, WI, USA). The detectors are set laterally with patients in the supine position and the velocity of the particle is subsequently calculated. Thirty-second dynamic images should be collected over a period of 20 minutes. To determine intratest reproducibility, the test can be repeated after 4-hour interval on the same day, using the same procedures and conditions. To determine interobserver and intra observer reproducibility, the data can be independently evaluated on at least two separate occasions. Following the test, the images can be evaluated to calculate NMTR in millimeters per minute (mm/min). The distance between the point where the radiopharmaceutical was applied and the point at which the radio particles reached the nasal cavity must be measured as a straight line using the imaging system. This distance was divided by the time elapsed to calculate the NMTR in mm/min [18]. The method has been modified by reducing the particle size to get rid of impairment of ciliary activity.

Although the measurement of mucociliary transport velocity by rhinoscintigraphy with 99mTc-MAA is considered to be a reliable measure of MCC by many physicians, no previous study has directly assessed the reproducibility of the test in human patients [18]. Further, a serious disadvantage of gamma scintigraphic experiments is the administration of radioactive

material which has numerous adverse effects on the general health. Damage to the lens of the eyes has been reported with repetitive nasal screening [19].

Mucus flow rate with 99m Tc-labelled resin particle

^{99m}Tc, obtained from a generator (Amersham, England) is used as radiotracer. The particles were Dower I-X4 (mesh: 50-100) anion exchange resin. Before the test, each subject should be given a complete ear-nose-larynx examination. The paranasal sinuses should be radiologically checked. Cigarette smoking is prohibited 1 h before the test. Nasal mucosa should be washed with 10 ml saline to clean out any foreign particles, scabs and thick mucus. The nose and nasopharynx should be then examined. Temperature and humidity are to be kept constant in the experiment room. All subjects are requested to rest in this room for 1 hour before the test. They are advised to breathe normally and not to cough, speak or move during the test. The subjects should be comfortably seated in a chair with a head-rest and remain stationary throughout the experiment. Three or four radioactive resin particles should be placed on the tragus and basal nose as marked for anatomical localization. This also aids in the calculation of the distance travelled by the particles from their original position by means of Polaroid pictures. The actual distance between the marks should be measured for each subject. A gamma camera (Pho-Gamma 111, Nuclear Chicago, Chicago, 111.) and a 1600 Multichannel Analyzer should be used to trace the movement of the particles. Between two and four radioactive resin particles (10-15 μ Cu) should be picked up with a microsurgical pick and placed on the upper surface of the lower concha, 0.5-0.8 cm behind the front part. A chronometer is started immediately. The movement of the particles is observed on the oscilloscopes. Polaroid pictures and 35-mm high contrast films are taken at intervals. The time at the beginning of the exposure and the exposure time must also be recorded. The experiment should be stopped when the particles reached the nasopharynx [20].

Mucus flow rate with radiopaque Teflon dicks

Sackner [21] introduced radiopaque teflon disks into the nose and the velocity of transport was computed from a roentgenographic image using a detection method called Fluoroscope image intensifier.

Mucociliary transit time with coloring substances

Dyes being simple and inexpensive have a great advantage in vivo [22-24]. A droplet or a particle filled or loaded with a strong dye such as indigo carmine is placed in the anterior part of the nasal cavity, so that the dye will subsequently be transported to the nasopharynx [1]. The time between the placement of the dye and its appearance in the pharyngeal cavity is measured. Repeated inspections of the pharyngeal cavity are necessary, which is inconvenient [1].

Mucociliary transit time with a combination of dye and saccharin

A mixture of charcoal and saccharin powder is used. The charcoal-saccharin tests are performed from 1 to 3 PM to eliminate the influence of circadian and nasal rhythms [25]. The end point

can be detected by the perception of sweet taste and appearance of the dye on pharyngeal inspection. This method eliminates the disadvantage of repeated inspections and influence of the taste threshold of the individual [1].

CONCLUSION

The techniques which involve radiolabelled particles and radio opaque disks require expensive equipments. It may involve the potential hazard of X irradiation, especially to the lens of the eyes, if nasal screening is used repeatedly. Saccharin test is inexpensive, non-invasive and has a great advantage of reproducibility. It can also be implemented in large number of samples. Further, it has been reported that the results of saccharin test are similar to those obtained using radiolabelled particles.

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