Measurment of Nasal Mucociliary Clearance by Saccharin Test

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Abstract

The nasal mucosa lines the entry of the respiratory tract and is in constant contact with a great variety of inhaled microbial antigens and allergens. Mucociliary clearance is defined as cleaning of upper and lower airway by interaction of nasal mucus and ciliary beating. Inhaled particles, bacteria and virus are trapped in the mucus and are transported by the beat of the cilia to the pharynx where they are either swallowed or coughed up.

The main purpose of this study is to examine the capabilities of the saccharin test and its application in determination of the modified mucociliary clearance time (MTC) by obstructive nasal breathing, caused by different local pathology. The essence of the test is that a small amount of saccharin is placed approximately 1 cm behind the anterior end of the inferior turbinate. In the presence of normal mucociliary action, the saccharin will be swept backwards to the nasopharynx and a sweet taste perceived.

15 healthy volunteers and 15 patients with obstructive nasal breathing were tested with the saccharin test. Most of the similar studies indicate different clearance times as normal, averaging between 5 and 19 minutes (max. 36 minutes). Results, out of the norm, were registered in cases with present nasal breathing disorder. Our research does not show considerable difference in this respect.

Regardless of whether normal or pathological mucociliary clearance is concerned, the saccharin test appears to be simple, inexpensive and reproducible examination, appropriate for quick and reliable valuation of mucociliary function or dysfunction.

Keywords: nasal mucsa, nasal mucociliary clearance, nasal function

Introduction

Mucociliary clearance is a key defence mechanism in human upper and lower airways, and its impairment predisposes to chronic infections of the nose, paranasal sinuses and respiratory tree [1].

MCC is defined as cleaning of upper and lower airway by interaction of nasal mucus and ciliary beating and its morphological substrate is the pseudostratified columnar ciliated epithelium of the nasal cavity. From this definition it is obviously that proper mucus transport depends on number, structure and function of the cilia as well as biochemical, physical and chemical properties of the mucus. Nasal mucus contains 90% water, glycoproteins and ions, and has two layers: the lower liquid layer, covered by the more viscous gel phase. Height of the liquid layers is important for the efficiency of the ciliary stroke [2]. Ciliary movement in itself is coordinated by metachronal waves, thereby coupling the beat of each cilium to that of neighbouring cilia [3]. The mucus-cilia interaction results in the fact that trapped inhaled particles and microorganisms are continuously transported towards the oropharynx, where they are swallowed or expectorated [4].

Many factors affect the MCC. Optimal MCC is achieved at 37°C and 100% relative humidity [2]. Mucus production can be increased or decreased by body hydration, temperature, humidity, nerve tissue stimulation, local

blood supply, hormones [5]. Acute upper respiratory tract infections may direct damage the cilia and change the rheological properties of the nasal secretions. Tobacco smoke has a ciliostatic effect and changes the viscoelastic properties of mucus [1]. Many researches have proved longer nasal MCC in smokers. Higher daily physical activity level is associated with better mucociliary function in healthy people and exactly the opposite in heavy smokers [6]. Environment pollutants such as nitrogen dioxide, sulphur compounds and ozone depress the mucociliary system [3]. Medicals can change mucociliary transport both ways – increasing or decreasing it. For example furosemide [4], benzodiazepines, aspirin, tertiary ammonium anticholinergics impair MCC, while corticosteroids, methylxanthines, adrenergic agonists, quaternary ammonium anticholinergics, amiloride and some antibiotics augment it [7]. Deterioration of MCC is observed in old age [2].

Aim

The main purpose of this study is to examine the capabilities of the saccharin test and its application in determination of the modified mucociliary clearance time (MCT) by obstructive nasal breathing, caused by different local pathology. Making our own examination we present the application of the test in the daily ENT practice. By comparison with other methods for investigation of MCC the authors intend to show the advantages of this test without to forget its limitations.

Materials and methods

Participants

There were two groups of subjects evaluated. Fifteen healthy volunteers in the age from 22 up to 59 years (10 males, 5 females) were examined and from their results we have made conclusions about the normal mean value of saccharin transit time. The second group includes fifteen patients (10 males, 5 females; age 18 to 65 years) with some nasal pathology. Ten of them had deviation of the nose septum, four were with nasal polyposis and one woman was polymorbid – she suffered from bronchial asthma, septal deviation and turbinate hypertrophy.

Methods

The saccharin test, first described by Andersen and modified by Rutland and Cole, consists in placing a particle 1 mm in diameter under direct visual control on the inferior nasal turbinate 1 cm from its anterior end [1]. The patients are not allowed to breathe deeply, talk, cough, sneeze or sniff [8], eat, drink and smoke. They are instructed to swallow only a few times per minute [8]. In the present of normal mucociliary action, the saccharin will be swept backwards to the nasopharynx and a sweet taste perceived [10]. We didn't specify the actual taste they were to expect in order to avoid false positives [9], so our patients were told to indicate any particular taste. In this research was used a modification of the saccharin test, applied in some other studies [5] – we replaced the particles with 2% solution of sodium saccharin, which shortens the transport time [2]. The time of first taste perception was recorded in minutes.

Some authors minimize the subjectiveness of the sweet perception by dipping the particle in a dye powder such as indigo blue. After the patient has felt the sweet taste, the investigator can verify the occurrence of a blue color in the nasopharynx. They also accentuate the need of standardized conditions by performing the test – temperature, humidity, way of placing the saccharin, acclimatization of the patient to the test room [11].

Materials

The set needed to perform the test is very simple. It consists of a head mirror, a light source, a 2-blade speculum, a cotton swab, a saccharin solution and a stopwatch.

Results

First were tested fifteen healthy volunteers: 10 males, 5 females; mean age 30 (from 22 to 59); two of them are ex-smokers, and three are present smokers. Their results were averaged and this mean value was considered as normal MCC. The range of values is from 3 to 15 minutes. Normal MCC, investigated by us, is 7.5 minutes. No significant differences are established between both genders or related to the age. Only four of the participants had MCC > 7.5 min (one complained about dry nasal mucosa, other two are ex-smokers, the fourth is smoker). Table 1. presents the distribution of the participants and their MCC times.

Table 1. Normal MCC (min)

	Range	Mean
Non-smokers	3-11	6,4
Ex-smokers	10-11	10,5
Smokers	6-15	9

One of the most common reasons for impaired mucociliary clearance is the increased nasal resistance. This fact directed our attention to patients with obstructive nasal diseases such as deviation of nasal septum and nasal polyposis. We examined 15 persons (10 males, 5 females) in the mean age of 38 years (from 18 to 65 years). Ten of them had deviations; four had polyps and one woman had deviation plus turbinate hypertrophy plus asthma.
The mean value of MCC measured by the 15 people with existing nasal disorder was 12 minutes. As a number it is not able to appraise the actual affection of MCC. The table below gives detailed information about the influence of the pathology on the rate of MCC.

Table 2. MCC by nasal desease

	Number of patients	MCC
Deviation of nasal septum	5	< 10 min.
	5	> 10 min.
Nasal polyposis	1	> 10 min.**
	1	> 30 min.*
	2	> 60 min.
Dev. + Turbinate hypertrophy	1	> 30 min.*

* The test was stopped after 30 min. under circumstances, beyond control of the authors.

Results less than 10 min. were received by patient with mild deviated septum or suffering from obstructed nasal breathing in the last few years (caused by trauma et al.). The man who showed any MCC (**) had also a mild form of polyposis, the rest of this group weren't able to perceive any taste, which might be due to change of taste sensation as a whole.

Discussion

MCC in other studies

Most of the similar studies indicate different clearance times as normal, averaging between 5 and 19 minutes (max. 36 minutes). With very little exceptions they demonstrate results, very close to ours, although they are performing the saccharin test, described by Rutland and Cole (particles saccharin, see above). A comparison between normal values, established by us and other authors, are shown on Table 3.

Table 3. Comparison between present study and other studies

	Normal MCC time (min.)
Present study	7.5
Proenca et al. [6]	8 (8-11)
Proenca et al.[8]	10 (6-14)
Corbo et al. [1]	8 (less than 24)
Stanley et al. [12]	11
The Asthma Center [5]	5-8
Goto et al. [4]	10-12
GPnotebook [10]	10-20
Plaza Valia et al.[9]	16 (12-20)
van Cauwenberge et al. [11]	22 (15-29)
Beule [2]	< 30

Proenca et al. make two studies [6, 8] about influence of tobacco smoke on the MCC and establish some relations: 1) smokers have slower MCC time than non-smokers; 2) immediately after smoking smokers show normal MCC, unlike after 8-hour pause, when MCC is considerably decreased; 3) impairment of MCC depends on the number of cigarettes per day – light smokers (up to 15 cigarettes/day) have normal MCC, moderate (16-25 cigarettes/day) and heavy smokers (>25 cigarettes/day) – reduced clearance. One of our smokers was measured after smoking; one woman is light and one is moderate smoker. Their results are compared in the next table.

Table 4. Influence of smoking on MCC

	Proenca et al.	Present study
30 min. after smoking	11±6	6
After 8-hour pause	16±6	-
Light smokers	9(7-11)	6
Moderate smokers	13(11-17)	15
Heavy smokers	13(10-21)	-

The results prove the negative influence of smoking on the function of nasal mucosa. Most important is that MCC is not only impaired by tobacco but it doesn't recover after interrupting smoking (ex-smokers' MCC > 10 min.).

Saccharin test and other methods

MCC can be measured by plenty of tests, most of them are complicated, slow and difficult to perform. Nuclear medical test with technecium 99 is based on moving radiolabelled particles, which requires

increased technical effort and comes along with radioactive contamination [2, 13]. As an option exist also tests with methylene blue [9] or titanium dioxide [2], although the use of larger, insoluble particles demonstrates considerable variation in flow rates [12]. In-vitro tests are available for measuring the MCC. Ciliary beat frequency (CBF) shows nearly ideal sensitivity and specificity, anyway it is time-consuming technique and only available in very few centers [2]. There is an excellent correlation between saccharin test on one side and CBF and NO levels on the other [11]. Compared to other methods for measuring the mucociliary transport saccharin test seems to be the simplest, most reliable, fastest and least expensive [9].

For exhaustiveness we will mention the disadvantages of the saccharin test like subjectivity, it is hard applicable to children, depends on the general taste perception and needs to be performed by standardized conditions.

Conclusion

Sharing the opinion of the authors we cited, we consider the saccharin test inexpensive, simple to perform in a large number of patients, reproducible, quick and reliable examination of mucociliary transport. We agree that this test should be used as screening test to detect abnormal mucociliary clearance [1, 13]. It is useful for scientific investigation of overall mucociliary function because of the established correlation between nasal and tracheobronchial MCC [9]. This makes the saccharin test irreplaceable in the daily ENT practice.

References:

[1] Corbo G M, Foresi A, Bonfitio P, Mugnano A, Agabiti N, Cole P J. Measurement of nasal mucociliary clearance. *Archives of Disease in Childhood*, 1989, 64: 546-550.

[2] Beule A G. Physiology and pathophysiology of respiratory mucosa of the nose and the paranasal sinuses. *GMS Current Topics in Otorhinolaryngology – Head and Neck Surgery* 2010, Vol. 9: Doc07. DOI: 10.3205/cto000071

[3] Houtmeyers E, Gosselink R, Gayan-Ramirez G, Decramer M. Regulation of mucociliary clearance in health and disease. European Respiratory Journal, 1999; 13: 1177-1188.

[4] Goto D M, Torres G M, Seguro A C, Saldiva P H N, Lorenzi-Filho G, Nakagawa N K. Furosemide impairs nasal mucociliary clearance in humans. *Respiratory Physiology & Neurobiology* 2010; 170; 3:246–252.

[5] Mucociliary clearance. *The Asthma Center Education and Research Fund.* http://www.theasthmacenter.org/index.php/disease_information/sinusitis/sinus_mechanism/mucociliary_clearance/

[6] Proença M, Pitta F, Kovelis D, Mantoani L C, Furlanetto K C, Zabatiero J, Ramos D, Ramos E M C. Transporte mucociliar e sua relação com o nível de atividade física na vida diária em fumantes saudáveis e não fumantes. *Revista Portuguesa de Pneumologia*, 2012; 18; 5: 233-238.

[7] Houtmeyers E, Gosselink R, Gayan-Ramirez G, Decramer M. Effects of drugs on mucus clearance. *European Respiratory Journal*, 1999; 14: 452-467.

[8] Proença M, Xavier R F, Ramos D, Cavalheri V, Pitta F, Ramos E M C. Efeito imediato e a curto prazo do cigarro sobre o transporte mucociliar nasal de fumadores. *Revista Portuguesa de Pneumologia*. 2011; 17:172–176.

[9] Valía P P, Valero F C, Pardo J M, Rentero D B, Monte C G. Saccharin Test for the Study of Mucociliary Clearance: Reference Values for a Spanish Population. *Arch Bronconeumol*. 2008;44(10):540-5.

[10] Saccharin test for nasal mucociliary clearance. *GP notebook*: http://www.gpnotebook.co.uk/simplepage.cfm?ID=-986382286.

[11] Van Cauwenberge P, Wang D Y, Ingels K, Bachert C. The nose. *Kugler Publications*, 1998;36-42.

[12] Stanley P J, Wilson R, Greenstone M A, MacWilliam L, Cole P J. Effect of cigarette smoking on nasal mucociliary clearance and ciliary beat frequency. *Thorax* 1986;41:519-523

[13] Stanley P, MacWilliam L, Greenstone M, Mackay I, Cole P. Efficacy of a saccharin test for screening to detect abnormal mucociliary clearance. *British Journal of Diseases of the Chest*. 1984; 78:62-65.