Nasal mucociliary clearance, nasal and oral pH in patients with insulin dependent Diabetes Mellitus

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Thirty-two patients with insulin-dependent diabetes mellitus(IDDM) were included in this study. Mean value of nasal mucociliary clearance and oral phi in patients with IDDM were statistically lower than those of healthy subjects(p<0.05). Nasal pH was found not to be affected. Mean values of nasal mucociliary clearance, oral and nasal pH in respect to the fasting glucose levels were evaluated and the only statistical difference was detected between the mean values of oral pH in patients with fasting glucose level below 11.1mmol/L and above 19.4mmol/L(p<0.05). When mean values of nasal mucociliary clearance, oral and nasal pH were evaluated in respect to hemoglobin A_{1c} values and the duration of the disease, no considerable difference was detected. Results of adult patients and children with IDDM were not statistically different, either. [Turk J Med Res 1997; 15(1):36-39]

Key Words: Nasal mucociliary clearance, Nasal pH, Oral pH

The diabetic patient is susceptible to a series of complications that cause morbidity and mortality. Major long-term complications include retinal, renal, neuronal and vascular involvement(l). Among miscellaneous abnormalities of diabetes mellitus, a number of rhinological problems take part. These include mucosal erosions, septal perforations and susceptibility to infections(2,3). To the best of our knowledge, there is only one study about nasal mucociliary clearance(NMC), nasal and oral pH in diabetes mellitus.

NMC is the first barrier of the tracheobronchial tree that potentially noxious particles must penetrate. Early studies of NMC were performed by Proetz and Hilding(4). A simple and non invasive method has been perfected by Anderson et al., consisting of depositing a particle of saccharin on the nasal mucosa and noting the time at which the subject reports the first taste of sweetness(3).

The aim of this study is to detect the nasal pathophysiological changes due to diabetes mellitus and to analyse these alterations in respect to fasting glucose level, hemoglobin A_{1c} (Hb A_{1c}), and the duration of the disease.

MATERIALS AND METHODS

Thirty-two non-smoking insulin dependent diabetic patients aged 7-65 years and 10 healthy subjects were included in this study. Patients with abnormal rhinological examination were excluded. The duration of the disease was reported, systemic physical and rhinological examinations were performed and fasting blood sugar and hemoglobin A_{1c} (Hb A_{1c}) were detected. NMC was measured by using saccharin. In this method a 1 mm. diameter particle of saccharin was placed on the surface of the inferior turbinate 1-1.5 cm. behind the anterior nares of the sitting subject. The subjects were asked to swallow once per 30 second to tell the time when they feel the sweet taste and not to sneeze or sniff during the test. Before the start of experiment the subjects spent approximately 30 minutes in a stable environment, similar to the test room, in order to minimize influences resulting from changes in temperature and humidity. The distance between the beginning of mucociliary membrane and the posterior wall of the pharynx was measured with a probe. In each subject, the ability to taste saccharin was checked by placing saccharin directly on the tongue. Oral and nasal pH was detected by an indicator paper(Universal-Indikatorpapier, pH 1-10, Merck).

For statistical analysis student's t test was used.

RESULTS

Thirty-two diabetic patients, aged 7-65 years, were included in this study. Mean age was 34.93+19.98. Fifteen(46.55%) were male and 16(53.45%) were female. Ten(31.25%) of them were younger than 15 years and the remaining 22(68.75%) were older.

Mean values of NMC, nasal and oral pH in diabetic and nondiabetic patients and their statistical differences were shown in Table 1 and Figure 1.

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Table 1. Mean nasal mucociliary clearance, oral and nasal pH in diabetic patients and non diabetic cases and the statistical comparisons between them.

	Diabetic patients n=32	Non diabetic cases n=10	p value
Mean NMC	5.17±1.98	7.19+2.30	<0.05
Mean oral pH	5.42±0.55	6.45±0.55	<0.05
Mean nasal pH	7.06±0.51	7.10±0.51	>0.05

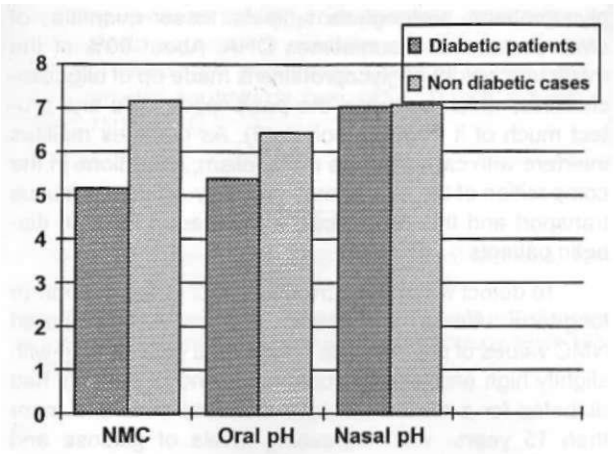

Figure 1. Comparison of mean nasal mucociliary clearance (NMC), oral pH and nasal pH values in diabetic and non diabetic subjects.

Table 2. Mean nasal mucociliary clearance, oral and nasal pH of patients in respect to their fasting glucose values.

	Glucose <11.1mmol/L n=8	Glucose 11.1-19.4mmol/L n=19	Glucose >19.4mmol/L n=5
Mean NMC	5.96±2.50	4.83H.68	5.25±2.20
Mean oral pH	6.0±0.59	5.23±0.42	5.20±0.27
Mean nasal pH	7.3U0.45	6.92±0.53	7.0010

Mean values of NMC, oral and nasal pH in respect to the fasting glucose levels were shown in Table 2. The only statistical difference was detected between the mean values of oral pH in patients with fasting glucose level below 11.1mmoi7L and above 19.4mmol/L(p<0.05). As the glucose level increased, oral pH decreased.

Mean values of NMC, oral and nasal pH in respect to Hb A_{1c} values of the patients were shown in Table 3. No statistical differences were detected between them.

Mean values of NMC, oral and nasal pH in respect to the duration of the disease were shown in Table 4. There was no statistical difference between them either.

Table 3. Mean nasal mucociliary clearance, oral and nasal pH of patients in respect to their HbA_{1c} values.

	Patients with HbA_{1c} <7% n=7	Patients with HbA_{1c} between 7-12% n=6	Patients with HbA_{1c}>12% n=19
Mean NMC	5.76±2.20	6.22±1.59	4.63+1.91
Mean oral pH	5.42±0.73	5.5±0.44	5.39±0.54
Mean nasal pH	7. 00±0	7.00±0	7.05±0.64

Table 4. Mean nasal mucociliary clearance, oral and nasal pH of patients in respect to the duration of the disease

	Duration < 5 years n=21	Duration 5-15 years n=6	Duration >15 years n=5
Mean NMC	5.06±2.14	5.37±2.25	5.41±0.99
Mean oral pH	5.47±0.48	5.58+0.86	5.00±0
Mean nasal pH	6.97±0.55	7.00±0	7.30±0.44

Table 5. Mean nasal mucociliary clearance, oral and nasal pH values of adults and children with diabetes mellitus.

	Adults n=22	Children n=10
Mean NMC	5.08±1.79	5.39±2.44
Mean oral pH	5.34±0.56	5.60±0.51
Mean nasal pH	7.00±0.55	7.10±0.31

Results of adult patients and diabetic children were shown in Table 5. Between these groups we detected no statistical difference.

Of patients five(15.6%) had foot ulcer, 10(31.25%) had retinopathy, one(3.12%) had neuropathy, four(12.5%) had nephropathy, four(12.5%) had hearing loss and three(9.37%) had atherosclerosis.

DISCUSSION

Nasal mucociliary transport efficiency depends upon interaction of two main factors: the ciliary beating of the epithelial cells and the physical properties of mucus secreted by serous and mucous glands(5,6). Studies of overall mucociliary function began in the 1830s, consisting mainly direct visualization of the rate of movement of a variety of substances applied to the mucosa(7). Now, electron microscopy and high-power phase-contrast microscopy are the most accurate tool for diagnosing ciliary abnormalities, but it is an invasive technique requiring biopsy of the respiratory mucosa. Except for them many methods were used to measure the nasal transit time. Among them, saccharin test has the major advantage of being simple to perform without sophisticated equipments).

In cases without diabetes we detected mean mucociliary clearance as 7.195±2.30 mm/min. Although the number of the non diabetic subjects were small, this mean value was consistent with mean NMC value in literature. From 1969 to 1990 many investigators found this value between 5.3-9 mm/min with average of 6.6 mm/min(7).

When compared to patients with IDDM mean NMC was statistically higher in normal subjects. The ciliated cells of upper and lower respiratory tracts, freely exposed to the external environment and the site of recurrent infections, would develop reactions to the noxious elements of this exposure. Changes of the axoneme or those in the basal bodies, ciliary rootless, or feet, equate with dyskinesia and mucostasis(8). Some significant landmarks in the study of cilia depended upon the introduction of electron microscopy, which was used to demonstrate the 9 plus 2 arrangement of internal fibrils in section of cilia, to discover subsidiary components of axoneme, to support a sliding-fibril hypothesis of ciliary bending, and combined with improved biochemical techniques, was used by Gibbon to show the localization of ATPase activity in dynein arms(9). Dynein is an ATPase protein that uses energy for ATP in performing cyclical shape changes that produce the active sliding movements^,9,10). In experimental models primacy of the polyol pathway in initiating neuropathy was proven by showing that inhibition of aldol reductase prevented the fall in tissue myoinositol content and decrease in ATPase activity(1). Speculatively decreased NMC in patients with IDDM may be attributed to this decreased ATPase activity.

The cause of diabetic complications is not known and may be multifactorial. In mammalian epithelia, there is evidence for nervous and hormonal control of mucous secretions, but although there are indications that an increase in mucous load stimulates ciliary activity, there is no convincing evidence of direct nervous or hormonal control of ciliary beat frequency(9).

Nerve stimulation causes secretion of mucus and this in turn mechanically stimulates ciliary beating. Seo reported that nerve stimulation produced a faster rate of beats and increased amplitude lasting 10 s or more; stimulation was accompanied by increased secretion of mucus, and Seo indicated that mechanical stimulation by this might accelerate the ciliary action(9). Poor stimulation due to neuropathy may probably is responsible of decreased NMC in patients with diabetes.

The possibilities of differential control of the constituents of mucus suggest that mucus transport could be varied by changes in the constitution or the amount of mucus that is secreted. Regulation of the hydration of the system through control of pH and ionic concentrations may also alter markings of the mucociliary escalator(9). In patients with diabetes, alteration of tissue pH may probably affect the property of mucus and thus mucus transport and ciliary activity may be impaired. Low nasal pH was not detected in diabetic patients but low oral pH. Nasal pH was higher but it was not statistically important. Higher nasal pH despite lower oral pH in diabetic patients can be attributed to the buffer system of nasal cavity. In the study of Yue(2), nasal cavity of diabetic patients were more alkaline too. And similar to our results, oral pH was more acidic.

Osmotic diuresis with loss of water and electrolytes may influence the hydration and thus may probably responsible for decreased NMC in diabetic patients.

Respiratory airway mucus is a complex mixture of glycoproteins, proteoglycans, lipids, lesser quantities of other proteins and sometimes DNA. About 80% of the molecular weight of glycoproteins is made up of oligosaccharides, which surround the polypeptide core and protect much of it from proteolysis(9). As diabetes mellitus interfere with carbohydrate metabolism, alterations in the composition of the mucus may probably influence mucus transport and this may result in decreased NMC in diabetic patients.

To detect whether decreased NMC is due to short or long-term effects of diabetes mellitus, we compared NMC values of patients with normal and high HbA_{1c}, with slightly high and high glucose levels and of patients had diabetes for a duration of less than one year and more than 15 years. With increasing levels of glucose and HbA_{1c}, it was observed that NMC had fallen. In contrast, patients with diabetes mellitus for more than 15 years had higher NMC than patients with diabetes less than one year. Although these differences are not statistical, consistency of the results can be attributed to the probability of decreased NMC being a short-term effect of diabetes mellitus. Increased NMC with increasing duration of disease confirms the other results.

When oral and nasal pH were evaluated in respect to glucose, HbA_{1c} levels and duration of the disease, it was observed that oral pH was the only that was affected. Oral pH was lower in patients with high glucose levels and high HbA_{1c} and lower in patients with diabetes mellitus over 15 years. Nasal pH was found to be independent of these parameters, probably due to buffer system of nasal cavity.

We additionally compared NMC values of diabetic adults and children. We could not find any difference. Similarly, no effect of ageing on the transport time of saccharin was detected in the study of Sakakura et 31(11).

Speculatively, we attributed decreased NMC in diabetic patients to probably decreased ATPase activity, poor stimulation due to neuropathy, osmotic diuresis with loss of water and electrolytes, and altered carbohydrate metabolism. With data analysis, although it seems to be a short-term effect of diabetes mellitus, studies on large series are needed. We believe the pathogenesis of this process will become obvious with electron microscopic studies on patients with diabetes mellitus.

İnsüline bağımlı Diabetes Mellituslu hastalarda nazal mukosilier klirens, ağız ve burun pH değerleri

Insülin bağımlı diabetes mellitus(IDDM) tartılı 32 olgu çalışma kapsamına alındı. IDDM tanısı almış olan hastaların ortalama nazal mukosilier klirens ve ağız pH değerleri sağlıklı gruptan anlamlı olarak düşük bulundu(p<0.05), ancak burun pH farkı saptanmadı. Açlık serum glukoz değerlerine göre değerlendirildiğinde, glukoz değeri 11.1mmol/L'nin altında ve19.4mmol/L üstünde olan olgularda yalnızca ortalama ağız pH değerinde istatistiksel fark saptandı(p<0.05). Hemoglobin A_{1c} değerlerine ve hastalığın süresine göre değerlendirme yapıldığında ise, ortalama nazosilier klirens, burun ve ağız pH değerlerinde fark saptanmadı. Çocuk ve erişkin hastaların değerleri arasında da fark yoktu. [T Klin Araştırma 1997; 15(1):36-39]

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