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Evaluation of the effects on nasal mucociliary clearance of various nasal solutions applied topically in patients with sinusitis

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Abstract

Mucociliary clearance (MC) is one of the main defense mechanisms of the nasal respiratory mucosa. The purpose of this study was to determine changes occurring nasal MC in patients with sinusitis, and how medical treatment affects changes in MC, and to identify an appropriate topical solution with positive effects on MC for use in the treatment of sinusitis by examining the effects of various topical solutions on MC. 60 patients diagnosed with rhinosinusitis at the ear, nose and throat clinic were included in this prospective study. Patients were randomly assigned into groups. Group 1 (n:10) received no topical treatment. Group 2 (n:10) was administered with fluticasone propionate, Group 3 (n:10) received mometasone furoate and Group 4 (n:10) received oxymetazoline. Group 5 (n:10) received isotonic sea water for nasal irrigation, while Group 6 (n:10) received isotonic Ringer's solution for nasal irrigation. Group 7 represented the control group (non-sinusitis). The saccharin test was used to determine nasal mucociliary clearance times. The saccharin test was performed before and on the 2nd week of treatment in all groups. Basal MCT and 2nd week MCT values were compared in all groups. When measurements performed 20 min and 14 days after administration of topical agents were compared with basal values, mean MCT values at 20 min. and 14 days were shorter in all groups compared to mean basal MCT values. However, the difference between 20-min, 14th day and basal MCT values was only statistically significant in the oxymetazoline and isotonic Ringer's solution groups ($p<0.05$). We think that oxymetazoline and isotonic Ringer's solution can be used as supportive therapy in the treatment of sinusitis since these produce a significant shortening of MCT.

Keywords: Nasal mucociliary clearance time, saccharin test, sinusitis

Introduction

Mucociliary clearance (MC) is one of the main defense mechanisms of the nasal respiratory mucosa. The effectiveness and speed of MC depend on such factors as coordinated ciliary activity, ciliary density, ciliary beat frequency, depth of the periciliary fluid layer, the amount of mucus and its viscoelastic characteristics [1]. In addition to acute or chronic pathological conditions, the nasal mucociliary system is also affected by various pharmacological agents. A defect in MC prolongs micro-organism contact with the cell surface and facilitates penetration into the cell. Respiratory system diseases such as rhinosinusitis and otitis may occur as a result [2].

Various topical nasal solutions are used in addition to antibiotics in the medical treatment of sinusitis. The use of those agents with

positive effects on nasal MC can enhance the effectiveness of treatment. It is therefore important to know the effects on MC of drugs administered by the nasal route.

The purpose of this study was to determine changes occurring nasal MC in patients with sinusitis, and how medical treatment affects changes in MC, and to identify an appropriate topical solution with positive effects on MC for use in the treatment of sinusitis by examining the effects of various topical solutions on MC.

Material and Methods

Patients diagnosed with rhinosinusitis at the ear, nose and throat clinic were included in this prospective study. A control group consisting of healthy individuals with no symptoms was also established. Informed consent was obtained from all participants. Local ethical committee approval was also granted for the study. Patients with allergy, known ciliary dysfunction disease, using sympathomimetic, parasympathomimetic or antihistaminic drugs, smokers, with a history of surgery or with obstruction findings at nasal examination were excluded.

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Diagnosis of sinusitis was based on anamnesis, determination of mucopurulent secretion at anterior rhinoscopic and endoscopic nasal examination, observation of mucopurulent secretion in the postnasal region at oropharyngeal examination, Waters view and paranasal sinus tomography.

Patients diagnosed with sinusitis were randomly assigned into groups. Seven groups were established, including a healthy control group. All patients received 875 mg amoxicillin and 125 mg clavulanic acid orally, twice daily, for 2 weeks.

Group 1 (n:10) received no topical treatment. Group 2 (n:10) was administered with 2 puffs of fluticasone propionate once daily into each nostril (for 2 weeks), Group 3 (n:10) received 2 puffs of mometasone furoate once daily into each nostril (for 2 weeks), and Group 4 (n:10) received 1 puff of oxymetazoline once daily into each nostril (for 5 days). Group 5 (n:10) received isotonic sea water and nasal irrigation into both nostrils 3 times a day (for 2 weeks), while Group 6 (n:10) received isotonic Ringer's solution and nasal irrigation 3 times daily into both nostrils (for 2 weeks). Group 7 represented the control group (non-sinusitis).

The saccharin test was used to determine nasal mucociliary clearance times (MCT). The test was applied to the side diagnosed with sinusitis based on clinical examination and imaging methods. When sinusitis was bilateral, the side with the more intense infection was selected, and the same side was used for all subsequent measurements. The test was performed at the same time of day, in the same room and by the same individual.

The test was performed at room temperature, with the patient in a seated position and after resting for 15 min. Internal nasal cleanliness was established by asking patients to evacuate their noses before the test. A $\frac{1}{4}$ saccharin tablet was placed 1-1.5 cm posterior to the anterior border of the lower concha. Patients were asked to swallow at 30-sec intervals and to report when a taste sensation occurred. The time to patients' experiencing a taste in the throat was measured using a chronometer. Patients were asked not to sniff or blow their nose, not to eat or drink anything, not to sneeze or cough and not to press their noses. The time between placement of the saccharin and its being tasted in the throat was defined as MCT. In the event that no taste sensation occurred after 30 min, the test was stopped and MCT was recorded as 30.

The saccharin test was performed before and on the 2nd week of treatment in all groups. In order to determine the early effects of topical agents in groups 2-6, in the first test (basal value measurement) we waited until the taste sensation entirely disappeared, and an additional test was performed 20 min after administration of topical agents. MCT was measured once in the healthy control group.

Control group MCT was compared with basal MCT values before treatment in the patients diagnosed with sinusitis. Basal MCT and 2nd week MCT values were compared in all groups. Basal and 20-min CT values were also compared in the groups receiving topical agents. Changes in pre- and post-treatment MCT were compared.

Statistical analysis was performed on SPSS software. All MCT values measured with the saccharin test were expressed as mean $\pm$ standard deviation. The Paired-Samples T test, One-Way ANOVA,

and the LSD multiple comparison test were used for statistical analyses. P values <0.05 were regarded as significant.

Results

Sixty patients with rhinosinusitis aged 18-60, 28 men and 32 women, and 30 healthy controls were enrolled in the study. There was no significant difference between the groups in terms of age or sex.

The mean MCT value of the control group was 9.7 ± 5.4 . Mean basal MCT before treatment in the patients with sinusitis was 17.1 ± 6.3 . The elevation in MCT in the patients with sinusitis was statistically significant when the two groups were compared (Figure 1).

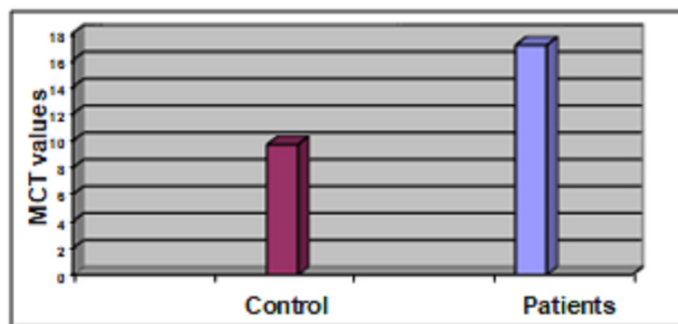


Figure 1. MCT values of patients and control group (MCT: Mucociliary clearance time).

Mean basal pre-treatment MCT in the patients with sinusitis was 17.1 ± 6.3 . Mean MCT in Group 1 on day 14 of treatment was 15.1 ± 6.3 . A statistically significant improvement was observed in mucociliary clearance with oral antibiotic ($p < 0.05$).

Basal, 20th minute and 14th day MCT values were summarized in Table 1. In the group receiving fluticasone propionate, basal MCT was 16.1 ± 2.9 , while MCT at 20 min was 15.3 ± 5.2 . In the mometasone furoate group, basal MCT was 16.0 ± 3.9 and MCT at 20 min was 15.1 ± 4.1 . In the oxymetazoline group, basal MCT was 17.9 ± 6.4 , while MCT at 20 min was 14.5 ± 5.1 . In the isotonic sea water solution group, basal MCT was 16.0 ± 4.3 and MCT at 20 min was 14.5 ± 2.9 . In the isotonic Ringer's solution group, basal MCT was 16.7 ± 4.9 , and MCT at 20 min was 13.0 ± 2.8 . When measurements performed 20 min after administration of topical agents were compared with basal values, mean MCT values at 20 min were shorter in all groups compared to mean basal MCT values. However, the difference between 20-min and basal MCT values was only statistically significant in the oxymetazoline and isotonic Ringer's solution groups ($p < 0.05$) (Figure 2).

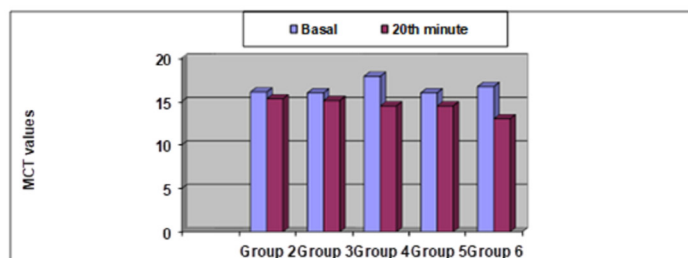


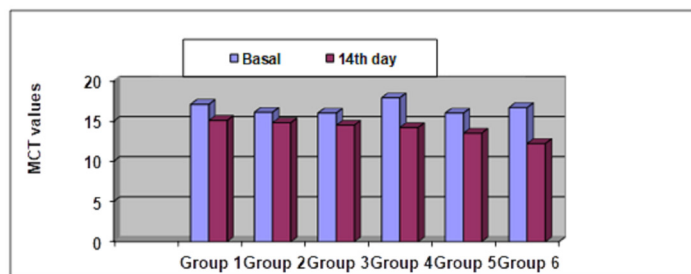
Figure 2. Changes in basal and 20th minute MCT values in patients with sinusitis (MCT: Mucociliary clearance time)

Table 1. Demographic Distribution

	Basal MCT	20th minute	14th day
Control	9.7 ±5.4		
Group 1	17.1±6.3		
Group 2	16.1±2.9	15.3±5.2	14.8±5.3
Group 3	16.0±3.9	15.1±4.1	14.5±3.7
Group 4	17.9± 6.4	14.5±5.1*	13.5±3.5*
Group 5	16.0±4.3	14.5±2.9	14.2±5.2
Group 6	16.7±4.9	13.0±2.8*	12.2±3.5*

*: Statistically significant

MCT values before treatment and on the 14th day of treatment in the groups receiving topical agents were 16.1±2.9 and 14.8±5.3, respectively, in the fluticasone propionate group, 16.0±3.9 and 14.5±3.7 in the mometasone furoate group, 16.0±4.3 and 13.5±3.5 in the isotonic sea water group, 17.9±6.4 and 14.2±5.2 in the oxymetazoline group, and 16.7±4.9 and 12.2±3.5 in the isotonic Ringer's solution group. When the two values were compared, no statistically significant difference was observed in the fluticasone propionate, mometasone furoate or isotonic sea water groups ($p>0.05$). However, the two values differed statistically significantly in the oxymetazoline and isotonic Ringer's solution groups ($p<0.05$) (Figure 3).

**Figure 3.** Changes in basal and 14th day MCT values in patients with sinusitis (MCT: Mucociliary clearance time)

Discussion

In our study, MCT was prolonged in patients with sinusitis compared to the control group. This prolongation shortened with treatment. MCT values were shorter at both 20 min and at 2 weeks compared to baseline in all the groups receiving topical solution. However, this shortening was only statistically significant in the oxymetazoline and isotonic Ringer's solution groups.

Antibiotics, nasal irrigation with saline solution, nasal decongestants and drugs such as topical nasal steroids are used for therapeutic purposes in sinonasal infections. How these solutions affect nasal MC is not fully understood. Investigation of the effects on MC of drugs administered by the nasal route is therefore important in terms of therapeutic efficacy.

Topical nasal decongestant drugs affect local mucosal blood flow, nasal air flow and ciliary movement in the epithelium of the nasal respiratory tract. Oxymetazoline is a commonly used nasal decongestant reported to reduce blood flow in healthy nasal mucosa by 50% [3]. The results of studies investigating the effects

of oxymetazoline on MCT are inconsistent. In a rabbit study, Min et al. observed no ciliary loss in any animals in the first and second weeks of oxymetazoline administration, but after the second week they reported ciliary damage in the mucosa of the maxillary sinus and MC impairment. They also emphasized that care was required during the use of topical nasal decongestants [4]. İnanlı et al. reported prolongation of MCT in patients with acute sinusitis, but observed that oxymetazoline significantly shortened MCT [5]. Van de Donk et al. reported that oxymetazoline and xylometazoline reduced the ciliary beat frequency in the mucosa of the sphenoid sinus but did not alter MCT [6]. We also determined that oxymetazoline shortened MCT both in the early period and after therapy. While positive results can be achieved when topical nasal decongestants are used properly, various rebound congestion and various histopathological changes in the nasal mucosa may occur.

Topical corticosteroids, whose main sphere of application is allergic rhinitis, are also used in the treatment of sinusitis. Meltzer et al. reported that the addition to antibiotics of twice daily mometasone reduced symptoms of sinusitis better than antibiotics alone [7]. Few studies have investigated the effect on ciliary functions of long-term nasal steroid use. Meltzer et al. reported that mometasone furoate nasal spray in seasonal allergic rhinitis caused a decrease in eosinophil, basophil and neutrophil numbers and a significant shortening in MCT [8]. We also observed that mometasone furoate reduced MCT, although the decrease was not statistically significant.

İnanlı et al. observed that fluticasone propionate administered topically for 3 weeks caused no improvement in MC in patients with acute sinusitis [5]. Similarly, Braat et al. reported no decrease in ciliary cells in mucosal specimens taken from the anterior part of the concha and no statistically significant difference in MC values following 6-week administration of fluticasone propionate in patients with allergic rhinitis [9].

Nasal irrigation is another method applied before nasal surgery and in the treatment of sinonasal disease. The aim of this treatment is to remove secretions, debris and crusts, to achieve mucosal healing and to reduce the risk of mucosal adhesions after surgery. Irrigation with saline solution has recently become increasingly used in the treatment of rhinosinusitis [10]. Talbot et al. determined that a buffered hypertonic saline nasal solution improved MC, but that physiological saline had no effect on MC [11]. Keojampa et al. showed that both buffered hypertonic and physiological nasal solutions improved nasal MC [12]. Homer et al. reported that saline solutions significantly shortened MCT. They also reported that it did this by altering the structural characteristics of mucus, rather than increasing the ciliary beat rate [13]. One study that used the saccharin test in patients with acute sinusitis compared pre-treatment MC values with those after 3 weeks of treatment and reported that isotonic saline solution had no effect on nasal MC, but that hypertonic saline (3%) significantly shortened MCT [5]. We also determined that isotonic saline produced a shortening in MCT, but that the decrease was not statistically significant.

Boek et al. compared the effects of NACI and Ringer's solutions at various concentrations on ciliary beat frequencies in human sinus mucosa in vitro using the photoelectric method. They concluded that 0.9% NaCl had moderate and temporary ciliostatic, that 7% NaCl exhibited complete but reversible effect and that 14.4% had

a complete and irreversible effect, but that Ringer's solution had no such effect effects. They also emphasized that Ringer's solution closely approximates to extracellular fluid and has no adverse effect on ciliary beat frequency, for which reason it is more suitable than saline for antral lavage, nebulization and nasal irrigation [14]. In an experimental study, Ünal et al. reported that Ringer's lactate solution had a more positive effect on MC than isotonic NaCl [15]. Another study observed a significant acceleration of nasal MC in patients undergoing nasal irrigation with Ringer's lactate for 3 weeks after nasal septal surgery compared to those using 0.9% NaCl [16]. In our study, we observed that isotonic Ringer's solution statistically significantly shortened nasal MCT both in the early period and at the end of 2-week treatment.

Conclusion

MC is slower in patients with sinusitis than in healthy individuals, and MCT is longer. The essential point in the treatment of sinusitis is to bring infection under control with a suitable antibiotic. However, some topical agents can be added to treatment due to their positive effects on nasal MC. We think that oxymetazoline and isotonic Ringer's solution can be used as supportive therapy in the treatment of sinusitis since they shorten the MCT significantly.

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