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Research Article

The Role of Local Treatment in Recurrent and Persistent Cases of Rhinisinusitis without Polyposis

Hany Amin[1]* and Ahmed Mohammed Abdelghany Abdelrahman[2]

[1]*Professor of Otolaryngology and Head and Neck Surgery, Benha University, Egypt*

[2]*Associate Professor, ORL Department, Benha University, Egypt*

***Corresponding Author:** Hany Amin, Professor of Otolaryngology and Head and Neck Surgery, Benha University, Egypt.

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Abstract

Introduction: The chronic non polypoidal rhinosinusitis is a frequent disease causing patients disability and repeated symptoms. The systemic treatment is not effective in many cases. Surgery is expansive and not suitable every patient. Mucociliary mechanism is affected by various conditions mainly temperature, ph, viscosity, osmolality, electrolytes, neural balance between sympathetic and parasympathetic systems, hormonal and local infection (biofilm).

Aim of the Study: So we are trying to focus on local treatment as a modality of treatment which can be used with the other types of treatment.

Method:PThis is a prospective single-blinded (clinician only) randomized controlled trial recruited patients with active CRS without polyposis. In this study we will compare several local treatment to evaluate its efficacy and potency through evaluating the local treatment changes on the mucociliary mechanism of the rhinosinusitis patients and in treating chronic rhinosinusitis.

As local antifungal, local antibiotic, saline nasal wash, local corticosteroids and honey compound. Evaluation of the mucociliary mechanism was done for all patients by estimating the mucous motility with saccharine test and one of its main content which is of utmost importance for nasal ciliary function which is the ph of the mucus.

However the ciliary action was estimated through scanning electron microscopy, The same procedures were repeated after 6 months of treatment.

Results: From these studies we had reached that the repetition of the results of different experiments gave a conclusion about the efficacy of the honey as a local treatment of our study cases.

Conclusion: Chronic rhinosinsitis does not affect the mucociliary system not only by the microbal affection and toxicity but also in changing the main factors which are responsible for its function.

Treatment should targeting all the altered factors that affect the mucociliary physiology we should pay more attention to local treatment as a modality of treatment that can deal with the multifactorial process of regaining a healthy mucociliary system.

Keywords: Mucociliary; Endoscopy; Chronic Disease

Background

According to a US national health interview survey of the prevalence of chronic conditions, CRS has been estimated to affect 12.5% to 15.5% of the total population, making it the second most common chronic condition in the United States [1,2].

An epidemiology study in Europe was conducted by The Global Allergy and Asthma Network of Excellence (GA2LEN) by sending questionnaires on The European Position Paper on Rhinosinusitis and Nasal Polyps (EPOS) criteria to a random sample of adults aged 15–75 years They found the overall prevalence of CRS was 10.9%, which confirmed the burden as a common chronic disease and pointed out the underestimation of this disease [3].

In another study at Egypt it was 9.9% of ENT patient in Kaluiobiat. It may significantly decrease quality of life [4].

Chronic rhinosinusitis is defined by the presence of at least two out of four cardinal symptoms (i.e., facial pain/pressure, hyposmia/anosmia, nasal drainage, and nasal obstruction) for at least 12 consecutive weeks, in addition to objective evidence. Objective evidence of chronic rhinosinusitis may be obtained on physical examination (anterior rhinoscopy, endoscopy) or radiography, preferably from sinus computed tomography [5].

Introduction

Anatomy and physiology of mucociliary system. The role of the nasal cavity is to humidify and warm the inspired air. Also, as the air passes through, the nasal cavity removes minute airborne particles and other debris before the air reaches the lower airways. Columnar epithelium lines the nasal cavity. This type of epithelial lining also secretes mucus that coats the lining and helps with the mucociliary clearance of minute aerosolized particles that become trapped in the nasal mucosa. The nasal cavity also functions to fa-

Table 1. American Academy of Otolaryngology–Head and Neck Surgery Diagnostic Criteria for Chronic Rhinosinusitis

The presence of at least two of the following cardinal symptoms for at least 12 consecutive weeks (listed in order of frequency):
Nasal obstruction
Nasal drainage
Facial pain/pressure
Hyposmia/anosmia
and
Objective evidence on physical examination (e.g., mucopurulent drainage, edema, polyps in the middle meatus) or radiography (preferably sinus computed tomography)

Information from reference 18.

Diagram 1

Source: [5].

cilitate drainage for the secretions from the adjacent paranasal sinuses. It also captures the odor bearing particles and transmits them to the olfactory recesses, that are in the superior portion of the nasal cavity, just medial to the superior turbinates. Air containing mucosal lined sinuses surround the nasal cavity, which includes the frontal, paired maxillary, sphenoid, and ethmoid sinuses. These cavities directly communicate with the nasal cavity. The secretions from these sinuses drain into the nasal cavity via the thin-walled ostia. Like the nasal cavity, the wall lining of the sinuses also secretes mucus. The cilia on the surface sweep the mucus in a carpet like fashion and move them towards the nasal ostia. The hard palate lines the floor of the nasal cavity. The lateral walls are spiral shaped mucosal folds that overlie the turbinates and sinus ducts draining into the ostia. The spiral shape of the turbinates is designed to increase the surface area for the inspired air [6].

Normal ciliated epithelium with goblet cells. Rhinosinusitis in hematopoietic stem cell-transplanted patients: influence of nasosinus mucosal abnormalities Figure A, Figure B [7].

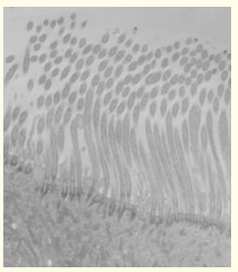

Figure A

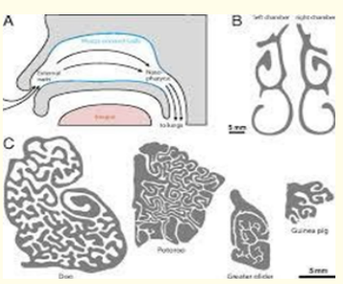

Figure B

Optimal mucociliary clearance is achieved at 37°Celsius and 100% relative humidity (absolute: 44 mg/dm3). Nasal Mucusisabout 10–15µm thick [8] and has two layers: the lower, 6 µm thick liquid layer (also called: periciliary liquid) is covered by the more viscous gel phase. The gel phase is structured by embedded mucin. Height of the liquid layers has tremendous effect of the efficiency of the Ciliary stroke [9]. Nasal mucus contains 90% water and glycoproteins as well as ions. It is produced by submucosal, seromucous glands, goblet cells, transudation of blood plasma, mucosal tissue fluid and tear fluid. Due to transudate, most proteins detectable in serum may also be demonstrated in nasal secretions. In cases of local inflammation, the amount of transudate and the irrespective proteins will increase.

Due to the coordinated, metachronous ciliary stroke, the mucus layer will be moved at a velocity of 2–25 mm/min [10]. In detail, control of the ciliary beat frequency is unknown. However, ciliary beat frequency will increase if cells are exposed to NO or a mechanical, calcium-mediated stimulus [11], whereas IL-13 will decrease the frequency [12]. In addition, intensive physical activity will decrease mucociliary clearance [13]. Particles bound to the mucus layer will be transported towards the pharynx passing the hiatus semilunaris. A second stream runs from the sphenoid sinus to the posterior ethmoid towards the choanae.

Within a paranasal sinus, mucociliary clearance will always be orientated towards the primary natural opening [14], while accessory ostia are by passed by the mucociliary clearance. Next to water and electrolytes, immune globulin (Ig) G and A can be detected in high concentrations in nasal mucus. Secretoric Ig-A (up to 80% Ig-A1; among others against Coxsackie viruses and poliovirus) is an obligatory ingredient and may provide up to50%of the total protein of nasal secretions [15]. It is secreted in to the tissue from plasma cells located near the basal membrane of the glands to bind and neutralize the antigen. Due to this effect, Ig-A is discussed as an important factor in pathogenic microbiological colonization of respiratory mucosa.

The average pH in the anterior of the nose is 6.40. The pH in the posterior of the nasal cavity was 6.27. The overall range in pH was 5.17-8.13 for the anterior cavity and 5.20 - 8.00 for the posterior cavity. The average baseline human nasal cavity pH is 6.3 [16].

The nasal passageway walls, and particularly the flap-like middle and inferior nasal conchae, are layered with respiratory mucous membranes secreted by goblet cells. These membranes have many small hair-like cells, known as cilia, that move mucus in waves toward the throat area. Bacteria, along with dust and other particles inhaled from the outside environment are snared by the nasal mucus, carried back out, and dripped into the gastric juices to destroy any possible pathogens. The mucus contains many defensive substances including lysozymes that dissolve and kill the bacteria, lactoferrin, immunoglobulins, and defensins, although some bacteria are not killed by this defensive substance.

In the infected person, it is known that the pH of the person changes accordingly, due to the presence of the bacterial community. During an infection, inflammation makes the pH of the mucus similar to that of plasma, 7.4. [17].

However the reactivation of this system by any means as surgery, systemic treatment or local treatment is the corner stone for eradication of this chronic disease.

Treatment is directed at enhancing mucociliary clearance, improving sinus drainage/outflow, eradicating local infection and inflammation, and improving access for topical medications. There may be a role for antibiotics in patients with evidence of an active, superimposed acute sinus infection. If medical management fails, endoscopic sinus surgery may be effective.

A recent attempts to treat Rhinosinusitis which is characterized by inflammation extending from the mucosa of the nasal cavity into the paranasal sinuses. There are some aggravating features, such as immunosuppression, that can cause the nasal mucosal inflammation to linger for a long period, resulting in chronic or recurrent episodes. Such immunosuppression is the major feature of patients undergoing a hematopoietic stem cell transplant (HSCT); rhinosinusitis prevalence is higher in this group compared to immunocompetent patients. Nasal epithelial abnormalities have been described in, and may have some influence over, recurrent sinus infections among those patients. However, it is not clear whether rhinosinusitis can trigger mucosal abnormalities or whether a preexisting vulnerability for sinusitis recurrence is more likely. The objective of the study was to verify the influence of rhinosinusitis on nasal epithelial damage in patients undergoing hematopoietic stem cell transplantation. HSCT patients, with and without rhinosinusitis, showed no significant histological abnormalities, except for ciliary disorientation and a possible decrease in ciliary and ultratructural abnormalities in HSCT patients with rhinosinusitis [7].

Gelardi and his colleagues said that biofilms were largely more frequent in patients with adenoid hypertrophy (57.4%), followed by nasal polyposis (24%), chronic rhinosinusitis (9.5%) and non-allergic rhinitis (7.6%). The results demonstrate that biofilm is present not only in infectious rhinitis, but also in inflammatory and/or immune-mediated diseases. The presence of biofilms significantly correlates with the degree of nasal obstruction as assessed by rhinomanometry [18].

Acute and chronic infections cause morphological changes in the respiratory mucosa. The ultrastructure of human respiratory mucosa was studied by scanning electron microscopy from the maxillary sinuses of 28 patients, with chronic sinusitis, from middle turbinates of 60 patients, with recurrent respiratory infections, and from healthy sphenoidal sinuses of 31 patients.

A loss of ciliated cells and an increasing number of nonciliated columnar cells with microvilli were seen in 62 per cent of the maxillary sinus mucosa. Ciliary disorientation was seen in 81 per cent of the chronically infected sinus mucosa and eight per cent in the healthy sphenoidal sinuses. Also metaplasia and extrusion of epithelial cells were prominent in chronic infections. Compound cilia were seen in 52 per cent of the Scanning electron microscopy findings of human respiratory cilia in chronic sinusitis and recurrent respiratory infections [19].

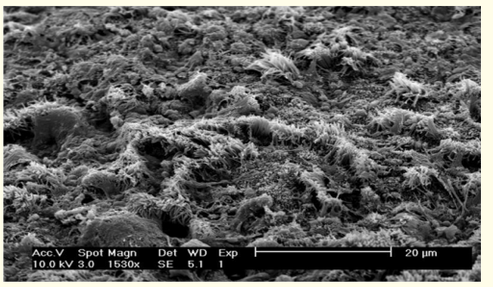

Figure C

Source: PubMedmples from patients with chronic sinusitis and in 31 per cent of the healthy sphenoidal sinuses. Short cilia were often seen in infected mucosa indicating ciliogenesis. OI: 10.1017/S0022215100130580.

The Effect of Cilia and the Mucociliary Clearance on Successful Drug Delivery is shown in diagram 2. Which reflects how local treatment can act [20].

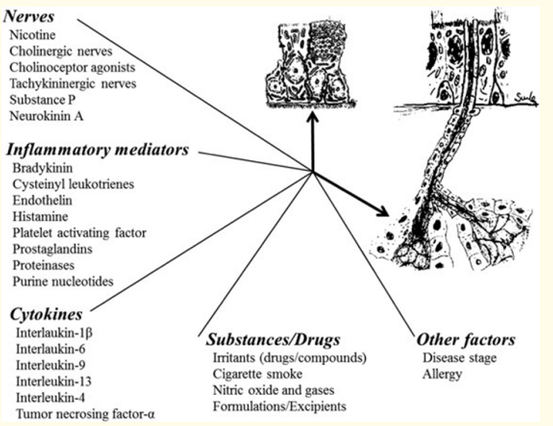

Diagram 2

Aim of the Study

The chronic non polypoidal rhinosinusitis is a frequent disease causing patients disability and repeated symptoms. the systemic treatment is not effective in many cases. Surgery is expansive and not suitable every patient. So we are trying to focus on local treatment as a modality of treatment which can be used with the other types of treatment. The main types of local treatment are compared in our study for evaluation of the mucociliary system before and af-

ter treatment. To know which is the most effective type for curing the mucociliary system and accordingly the chronic rhinosinusitis.

Methods

This is a prospective single-blinded (clinician only) randomized controlled trial recruited patients with active CRS without polyposis it was done in the period from January 2016 to June 2019 at Benha Medical School.

Local ethical committee approval was granted for the study. Patients with allergy, known ciliary dysfunction disease, using sympathomimetic, parasympathomimetic or antihistaminic drugs, with a history of surgery or with obstruction findings at nasal examination were excluded.

All patient will be undergone the following before followed in our study:

1. Full history
2. Full general examination and blood investigation
3. E.N.T examination.
4. Diagnostic nasal endoscopy.
5. C.T. scan on P.N.S.

The patient were diagnosed as having chronic sinusitis according to the criteriae of the American Academy of Otolaryngology and Head and Neck surgery [5].

In which the patients were divided into control and study group. The study group is divided into 5 subgroups each subgroup is formed from 25 to 30 patients and the control 20 patients. N.B according to patients reliability to the study treatment some of the patients were excluded.

In this study we will compare several local treatment to evaluate its afficacy and potency through evaluating the local treatment changes on the mucociliary mechanism of the rhinosinusitis patients and in treating chronic rhinosinusitis.

As local antifungal, local antibiotic, saline nasal wash, local corticosteroids and honey compound.

All patients participated in the study were informed of the study procedure and signed written consent forms.

- **The control group:** Are patients were complaining from chronic rhinosisnusitis who fit the criteriae of the American academy of otolaryngology and head and neck surgery of chronic rhinosinusits, at the beginning of the study. They were not receiving any treatment especially local treatment for 6 months before chosen as patients in our study
- **The study group:** Are also patients who are patients were complaining from chronic rhinosisnusitis who fit the criteriae of the American academy of otolaryngology and head and neck surgery of chronic rhinosinusitis. They were divided according to local treatment only given during 6 months
- **Study subgroup A:** Patients who received local antifungal treatment in the form of amphotericin B spray. Patients were instructed to instill by nasal spray 2 mL amphotericin B (300 mug/mL) to each nostril twice daily for 6 months.
- **Study subgroup B:** Who received local antibiotic treatment in the form of levofloxacin in the 100/5ml by nasal irrigation through nasal spray. The treatment is taken 10 days per month for 6 months.
- **Study subgroup C:** Who received local saline solution treatment in the form of hypertonic saline 2%, 1.5 cc in each nostril by nasal spray per puff 3 times daily.
- **Study subgroup D:** Who received local corticosteroids treatment in the form of mometasone 50 mcg/inhalation twice daily in each nostril for 6 months
- **Study subgroup E:** Who received local honey compound treatment in the form of clover honey diluted by 50% in distilled water. And applied by nasal spray 1 c.c in each nostril once daily for 6 month taken once in the morning.

Mucociliary mechanism is affected by various conditions mainly temperature, ph, viscosity, osmolality, electrolytes, neural balance between sympathetic and parasympathetic systems, hormonal and local infection (biofilm).

Some of these factors are more potent and more effective than the others.

Evaluation of the mucociliary mechanism was done for all patients by estimating the mucous motility with saccharine test and one of its main content which is of utmost importance for nasal ciliary function which is the ph of the mucus.

However the ciliary action was estimated through scanning electron microscopy, The same procedures were repeated after 6 months of treatment.

The mucus evaluation is done through

Sacharine test

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 saccharin tablet 1mm was placed 1 cm posterior to the anterior border of the lower concha. Patients were asked to swallow normally 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 the patient considered still affected by the disease [21].

Nasal ph evaluation

The test was performed at room temperature, in another setting, 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.

Using a portable pH meter and a glass-tipped probe nasal pH was measured in the inferior meatus in patients.

The ciliary evaluation

However the evaluation of the cilia was done with scanning electron. Microscopy in a sample of 5 patient. Before the treatment, samples for scanning electron microcopy (SEM) were taken from each patient in the form of small (2–3 mm in diameter) nasal mucosal biopsies from the anterior medial portion of the left inferior turbinate. Patients were choose randomly from the control and each subgroup.

The SEM samples were first immersed in 1% glutaraldehyde for fixation. Then, the samples were dehydrated in a graded alcohol series. Finally, the samples were immersed in hexamethyldisilane for 15 minutes at room temperature and air dried overnight. The samples were glued on the SEM specimen stubs with carbon glue.

We measured the ciliary area (C/A) by: Five photomicrographs original magnification x 1000 were taken at random for each specimen using SEM the ciliary area (C/A) that had been circled by hand in a picture was automatically calculated. The C/A was expressed as a percentage reflecting the ration of C/A in a given area.

Normal mucosa had ciliary area 88 -100%. while cases with rhinosinusitis showed that ciliary area ranging from 24-34% were considered as severe pathology. while moderate pathology showed that ciliary area 44-56%. However rhinosinusitis with mild pathology showed that ciliary area 66- 78%. Comparing this pretreatment findings with posttreatment [22].

Results

Table 1 shows the age range, gender percentage of the control group and the study subgroups.

All Patients, N=145	Control group N=20	Study subgroup A, N=25	Study subgroup B, N=25	Study subgroup C, N=25	Study subgroup D, N=25	Study subgroup E N=25,
Age, years, (range)	18-47	18-55	18-51	18-55	18-45	18 -53
Male, no. (%)	48%	36%	44%	60%	44%	52%
Female, no. (%)	52%	64%	56%	40%	56%	48%

Table 1

Mucous evaluation

Saccharine test

Saccharin test time in minutes	Control group Mean (SD)	Study subgroup A Mean (SD)	Study subgroup B Mean (SD)	Study subgroup C Mean (SD)	Study subgroup D Mean (SD)	Study subgroup E Mean (SD)
Pre treatment evaluation	19(47)	21.46(.35)	22.96(1.31)	23.11(35)	21.7(1.77)	22.11(.23)
Post treatment evaluation	-	20.07(.035)	19.57(.01)	19.07(.01)	21.07(4.99)	19.07(67)
Statistical significant	NS	NS	NS	S	NS	S

Table 2

A. The t-value is 1.72078. The p-value is .227432. The result is not significant at $p < .05$. **B.** The t-value is 4.16492. The p-value is .053098. The result is not significant at $p < .05$. **C.** The t-value is 5.32466. The p-value is .033508. The result is significant at $p < .05$. **D.** The t-value is 0.07615. The p-value is .946232. The result is not significant at $p < .05$. **E.** The t-value is 4.52173. The p-value is .045591. The result is significant at $p < .05$.

pH measurement

Ph evaluation for chronic rhinosiusitis	Control group (mean)	Study subgroup A	Study subgroup B	Study subgroup C	Study subgroup D	Study subgroup E
Pretreatment evaluation	6.35(.6)	7.35 (.4)	7.48(.35)	7.85(.47)	7.41(.26)	7.386.28)
Posttreatment evaluation	-	7.15(.32)	7.60(.67)	7.55(.42)	7.46(.83)	7.15(.22)
Statistical significant		NS	NS	Moderate S	NS	High S

Table 3

A. The t-value is 2.82843. The p-value is .052786. The result is not significant at $p < .05$. **B.** The t-value is 2.10494. The p-value is .084971. The result is not significant at $p < .05$. **C.** The t-value is 4.24264. The p-value is .025658. The result is significant at $p < .05$. **D.** The t-value is -0.18633. The p-value is .434686. The result is not significant at $p < .05$. **E.** The t-value is 29.69849. The p-value is .000566. The result is highly significant at $p < .05$.

Ciliary evaluation

By scanning electron microscopy

Control Figure 1 while moderate pathology showed that ciliary area 44- 56%.

Figure 1

Figure 2 for study subgroup A pre treatment showed ciliary area 60-65% mild pathology.

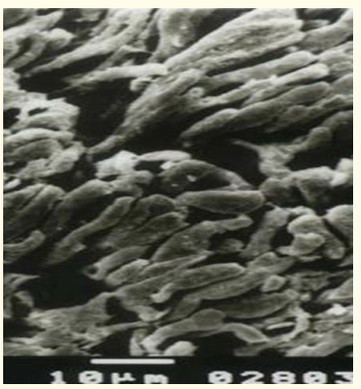

Figure 2

Figure 3 for study subgroup A post treatment mild pathology showed that ciliary area 66-72%.

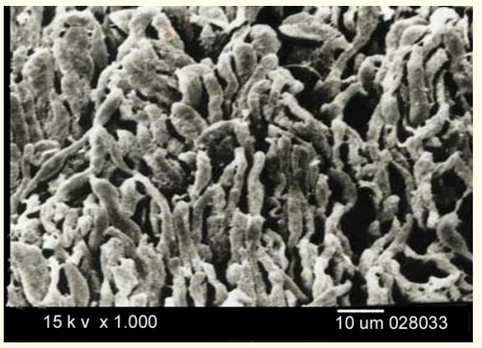

Figure 3

Figure 4 for study subgroup B pre treatment mild pathology showed that ciliary area 66- 68%.

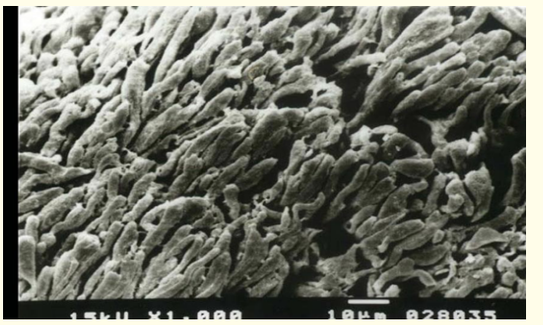

Figure 4

Figure 5 for study subgroup B post treatment mild pathology showed that ciliary area 69- 78%

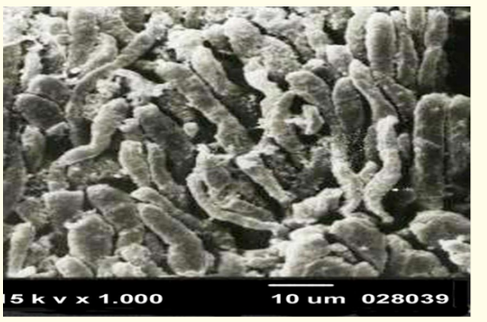

Figure 5

Figure 6 for study subgroup C pre treatment while moderate pathology showed that ciliary area was 44-56%.

Figure 6

Figure 7 for study subgroup C post treatment mild to moderate pathology showed that ciliary area was 58 -67%.

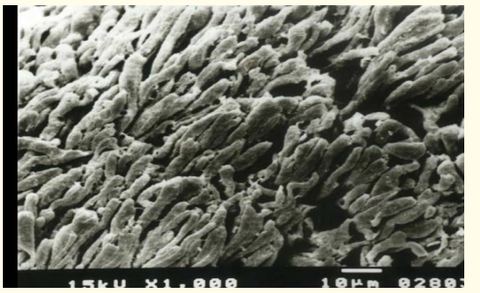

Figure 7

Figure 8 study subgroup D pre treatment showed ciliary area 60-65% mild pathology.

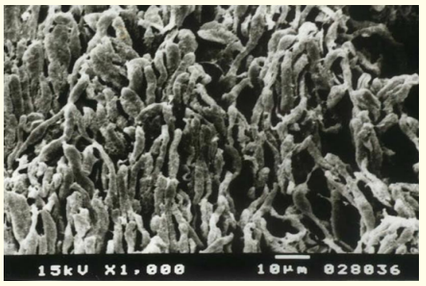

Figure 8

Figure 9 study subgroup D post treatment showed ciliary area 66- 68% mild pathology.

Figure 9

Figure 10 study subgroup E showed pretreatment severe pathology 37-43% ciliary area.

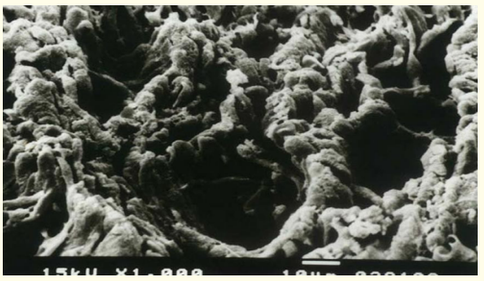

Figure 10

Figure 11 study subgroup E showed post treatment mild to normal pathology 80-91% ciliary area.

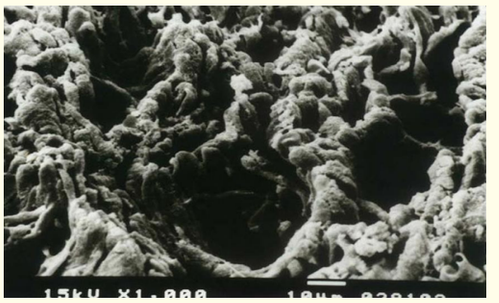

Figure 10

Figure 11 study subgroup E showed post treatment mild to normal pathology 80-91% ciliary area.

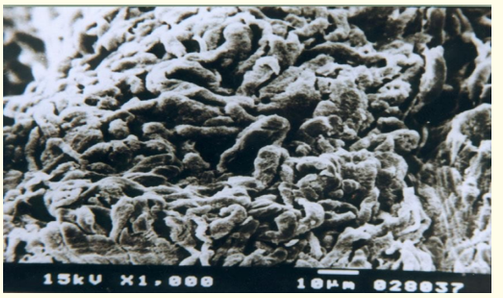

Figure 11

Discussion

Mucociliary system is important and should be considered as a potent air way defense mechanism for infections.

Recurrent or repeated upper respiratory tract infection mostly is due to temporary affection of hemostasis of this system rather than permanent infection of this system alone.

The change of nasal mucosa ph, viscosity, osmolality and local toxins may be the cause or causes of the decrease of efficiency of this system which cause the chronicity of the disease.

In this study we focused on local treatment for chronic non-polypoidal rhinosinusitis aiming to reduce symptoms, inability of patients to work and to find another cheap modality for treatment beside systemic medications and surgery.

	Pre treatment			Post treatment			
Degree of pathology	**Mild**	**Moderate**	**Severe**	**Normal**	**Mild**	**Moderate**	**Severe**
Control group		5				5	
Study subgroup A	2	2	1		1	3	1
Study subgroup B	4	1			4	1	
Study subgroup C		4	1		2	3	
Study subgroup D	3	2			4	1	
Study subgroup E		2	3	3	2		

Table 4: Number of patients regarding the pathology of each group.

Ciliary area percentage	Control group	Study subgroup A	Study subgroup B	Study subgroup C	Study subgroup D	Study subgroup E
Pretreatment evaluation	44-56%	51-55%	66-68%	44-56%	60-65%	37-43%
Posttreatment evaluation		48-50%	70 -72%	58-67%	66-69 %	80-91%
Statistical significant		NS	NS	Mild S	NS	High S

Table 5: Average of percentage of Ciliary damage of each group compared statistically.

Testing the mucociliary system efficacy before and after treatment was our indicator of recommending the kind of local treatment.

The saccharine test was prolonged in all our groups as they are diseased subjects. After the treatment some of them return towards normal so the test value are reduced but vary with different subgroups.

The mucous clearance was examined by using the saccharine test. We found that group E was the most group that had decreased values.

Followed by group C which was slightly different. In the other groups A,B and D the changes were non- significant.

The mean nasal mucociliary clearance rates were 11.1 mm/min for children and 12.7 mm/min for adults. Deviated nasal septum, chronic sinusitis, allergic rhinitis, atrophic rhinitis, chronic smokers and patients with recent nasal packings were taken as diseased conditions in adults, whereas children with adenoid hyperplasia were taken for the study. In all of these, nasal mucociliary clearance was significantly prolonged" [23].

MCT in control group was 6.61 ± 0.84 minutes, in unilateral (u/l) polypoidal sinusitis 13.45 ± 2.07 minutes, in bilateral (b/l) polypoidal sinusitis 21.31 ± 0.76 minutes, u/l non-polypoidal sinusitis 9.54 ± 1.00 minutes and in b/l non-polypoidal sinusitis 11.34 ± 0.93 minutes [24].

The following values for nasal MCT were obtained for the sample as a whole: mean (SD), 17.17 (8.43) minutes; median (interquartile range), 16 minutes (12-20 minutes), indicating that the central 50% of the sample fell within this 8-minute range; and maximum and minimum values of 4 to 54 minutes (range, 50 minutes). The upper and lower limits of normal were 6 and 36 minutes, respectively. In addition, it is noteworthy that only 6 subjects had a nasal MCT longer than 36 minutes [25].

In another study 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 [26].

Some factors like GERD are also factors rather than infection that can alter the saccharine test results. As in Deleyahe., et al. who stated that Thirty-seven (74%) patients showed a significant increment in their saccharin test values in comparison with the others subjects (23.79+/-5.58 vs 8.15+/-2.06min; P=0.0001). This group of patients reported only typical gastroesophageal symptoms (GES) without any other complaint.

Gastroesophageal endoscopic findings revealed some interesting and unexpected results in this subgroup [27].

Another factor which is smoking also play a role the mean MCC value was 23.59 ± 12.41 in the smoking group, 12.6 ± 4.67 in the passive smoking group, and 6.4 ± 1.55 in the healthy group. The comparison of MCC values between the smoking group and passive smoking group and between the smoking group and healthy group revealed statistically significant differences ($P < .01$). as stated by Habesoglu., et al. [28].

Although there is difference in the saccharine results that it makes its validity alone is questioned but, in our study, we are comparing the results of our patients with themselves.

Another important factor in testing the mucous clearance system is the ph measuring to test its efficiency.

Both ciliary function and mucus viscosity have been shown to be pH dependent [29]. In spite of the research based interest in nasal mucosal pH, measurement of nasal mucosal pH has never taken on clinical significance. This is likely because of the time – consuming nature of the procedure [30].

Moreover, the strong dependence of mucus physicochemical properties on environmental factors such as ionic strength and pH might impose additional complications to drug delivery systems [31].

The nasal mucosal pH is ≈ 5.5–6.5, and increases in rhinitis to 7.2–8.3. This knowledge has not led to the widespread measurement of the nasal mucosal pH as an objective clinical parameter. which agree with our results [32].

We found that group E was more significant in returning of its patient to acidity. Followed by group C which was slightly significant. The other groups A, B and D. were non- significant.

Also our results was consistent with the preoperative results of the ph in Kim., et al. study. The mean (± SD) nasal pH was 6.5 ± 0.5 (5.9 to 7.3) in 19 normal subjects, and 6.7 ± 0.6 (5.3 to 7.6) in 19 CRS patients before surgery, which showed no significant difference between the groups. The nasal pH values were in the range of 3.8–7.7 (mean ± SD 5.7 ± 0.9) at 3 months after surgery, and significantly lower than the preoperative values in patients (P = .004). The patients showing pH lower than 6.0 accounted for 10.5% before surgery, but 68.4% after surgery [33].

In spite of the cost and sophisticated maneuver of the scanning electron microscopy still it is an accurate and objective method for evaluation of cilia morphology and number. But it cannot be used as a routine test Chronic rhinosinusitis have evidenced by scanning electron microscopy to had ciliary impairment.

Patients with chronic sinusitis of uncertain origin exhibit a prominent loss of differentiated epithelial cells, as well as ciliary defects, most of which are likely to be secondary to the chronic disease process. These changes slow down mucociliary clearance and lead to a vicious cycle leading to chronicity [34].

A loss of ciliated cells and an increasing number of nonciliated columnar cells with microvilli were seen in 62 per cent of the maxillary sinus mucosa. ciliary disorientation was seen in 81 per cent of the chronically infected sinus mucosa and eight per cent in the healthy sphenoidal sinuses. Also metaplasia and extrusion of epithelial cells were prominent in chronic infections. Compound cilia were seen in 52 per cent of the samples from patients with chronic sinusitis and in 31 per cent of the healthy sphenoidal sinuses. Short cilia were often seen in infected mucosa indicating ciliogenesis [19].

The same results was obtained for ciliary function using the scanning electron microscopy. Improvement in Ciliary morphology and number in group E with less improvement in group C. and no changes in the other groups.

From these studies we had reached that the repetition of the results of different experiments gave a conclusion about the efficacy of the honey as a local treatment of our study cases. Which is consistent with these results.

The immune modulatory property is relevant to wound repair too. The antimicrobial activity in most honeys is due to the enzymatic production of hydrogen peroxide. However, another kind of honey, called non- peroxide honey, displays significant antibacterial effects even when the hydrogen peroxide activity is blocked. Its mechanism may be related to the low pH level of honey and its high sugar content (high osmolality) that is enough to hinder the growth of microbes.

Our results are the same as Lee., et al. who stated that forty-two patients were analyzed (MH, n = 20; SAL, n = 22). The SNOT-22 change score achieved a clinically significant improvement in both groups but was similar between MH (median [interquartile range]: -12 [-20, -1]) and SAL (-12.5 [-22, -6]) (p = 0.57). Culture negativity was better on MH (8/19, 42%) compared to SAL (4/21, 19%), nearing statistical significance (p = 0.11). Lund-Kennedy endoscopic change score improved in both groups but was not statistically better on MH (-3 [-5, 0]) compared to SAL (-1 [- 2, 0]) (p = 0.20). For patients not receiving oral antibiotics/steroids, culture negativity was statistically better on MH (5/10, 50%) compared to SAL (0/6, 0%) (p = 0.04). MH was well-tolerated. No adverse events were reported [35].

Thyme honey nasal spray seems to be a low-priced potential adjuvant remedy with excellent safety profile, to reduce inflammation and polyp formation and also fostering mucosal healing for patients suffering from chronic rhinosinusitis [36].

The results of the safety assessment, for normal sinuses treated with MGO alone or with MH/MGO (≤1.8 mg/mL) showed normal pseudostratified epithelium and cilia structure; however, higher concentrations caused cilia denudation and squamous metaplasia. As for efficacy, when compared to saline flush, treatment with MH/MGO at 0.9 mg/mL (0.608 ± 0.110 vs 0.316 ± 0.197 μm(3)/μm(2), respectively; p = 0.015) and 1.8 mg/mL (0.676 ± 0.079 vs 0.114 ± 0.033 μm(3)/μm(2), respectively; p = 0.001) significantly reduced biofilm biomass [37].

The antibacterial nature of honey is dependent on various factors working either singularly or synergistically, the most salient of which are H_2O_2, phenolic compounds, wound pH, pH of honey and osmotic pressure exerted by the honey. Hydrogen peroxide is the major contributor to the antimicrobial activity of honey, and the different concentrations of this compound in different honeys result in their varying antimicrobial effects. It has further been reported that physical property along with geographical distribution and different floral sources may play important role in the antimicrobial activity of honey [38].

Clover and other types of honey have antiviral and antibacterial effects. In a study comparing the antibacterial capacity of 16 differ-

ent types of honey, the clover variety had the strongest antibacterial action against harmful Staphylococcus aureus cells — equivalent to a 2.2 mg dose of the antibiotic kanamycin [39].

Regarding other topical treatment the only local treatment that was following local honey in its efficacy was pressurized high concentrated saline.

Chong., et al. agree with ours with difference of the volume administrated. The evidence suggests that there is no benefit of a low-volume (5 ml) nebulised saline spray over intranasal steroids. There is some benefit of daily, large-volume (150 ml) saline irrigation with a hypertonic solution when compared with placebo, but the quality of the evidence is low for three months and very low for six months of treatment. said that [40].

Using corticosteroids only and local antibiotics also only did not had significant difference in our study.

While Head., et al. stated that systemic antibiotics plus saline irrigation and intranasal corticosteroids versus placebo plus saline irrigation and intranasal corticosteroids One study (60 participants, some with and some without polyps) compared a three-month course of macrolide antibiotic with placebo; all participants also used saline irrigation and 70% used intranasal corticosteroids. Disease-specific HRQL was reported using SNOT-22 (0 to 110, 0 = best quality of life). Data were difficult to interpret (highly skewed and baseline imbalances) and it is unclear if there was an important difference at any time point (low quality evidence). To assess patient-reported disease severity participants rated the effect of treatment on a five-point scale (-2 for "desperately worse" to 2 for "cured") at the end of treatment (three months).

For improvement in symptoms there was no difference between the antibiotics and placebo groups [41].

Similar to many studies, the use of topical antifungal treatment for patients with CRS was not shown to be significantly effective. However, further studies are needed to obtain high levels of consistent evidence in order to arrive at a decision whether antifungal

Conclusions

Mucociliary lining of the nose is a dynamic system. It is controlled by many factors as ph, osmolality, concentration of electrolytes, viscosity, amount of mucous and presence or absence of microbes…etc. Ciliary number and vitality is crucial in the integrity of this system.

Chronic rhinosinsitis does not affect this system not only by the microbal affection and toxicity but also in changing the main factors which are responsible for its function.

Treatment should targeting all the altered factors that affect the mucociliary physiology we should pay more attention to local treatment as a modality of treatment that can deal with the multifactorial process of regaining a healthy mucociliary system.

Clover honey is an effective cheap and safe treatment for chronic rhinosinusitis. Followed by normal saline irrigation.

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