

Original Research Article

Evaluation of nasal mucociliary clearance in rheumatoid arthritis: a comparative analysis using saccharin test

Shelja Deswal^{1*}, Jyoti Yadav¹, Mohit Deswal², Harpreet Singh³

¹Department of Physiology, Pt. B.D. Sharma, PGIMS, Rohtak, Haryana, India

²School of Psychology and Public Health, La Trobe University, Melbourne, Australia

³Department of Medicine, Pt. B.D. Sharma, PGIMS, Rohtak, Haryana, India

Received: 11 September 2017

Accepted: 07 October 2017

*Correspondence:

Dr. Shelja Deswal,

E-mail: docshelja27@gmail.com

Copyright: © the author(s), publisher and licensee Medip Academy. This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

ABSTRACT

Background: Rheumatoid arthritis (RA) is a chronic multisystem disease of unknown etiology characterized by persistent inflammatory synovitis, usually involving peripheral joints in a symmetric distribution. RA is a systemic disease often associated with cutaneous and organ-specific extra-articular manifestations the mucociliary clearance system protects the lower respiratory system by trapping and removing inhaled pathogenic viruses and bacteria, in addition to nontoxic and toxic particulates (e.g., pollen, ash, mineral dust, mold spores, and organic particles), from the lungs. Effective clearance requires both ciliary activity and the appropriate balance of periciliary fluid and mucus.

Methods: This was a case control study conducted in the Department of Physiology, Pt. B.D. Sharma PGIMS, Rohtak in 50 females of age group 30-50 years. Control group comprised of 25 healthy volunteer females while study group comprised of 25 rheumatoid arthritis female patients with disease duration of more than five years. Proven cases of RA (as per 1987 ACR criteria) were taken with disease duration of more than five years from Rheumatology clinic of Pt. B.D. Sharma PGIMS, Rohtak. Nasal mucociliary clearance time was evaluated by saccharin method.

Results: The results of our study showed abnormal mucociliary clearance in rheumatoid arthritis patients.

Conclusions: The study shows an abnormal mucociliary clearance in rheumatoid arthritis patients. Impairment of mucociliary clearance seems to be the result of qualitative and quantitative alterations in respiratory secretions.

Keywords: Joints, Nasal mucociliary clearance, Rheumatoid arthritis, Saccharin

INTRODUCTION

Rheumatoid arthritis (RA) is a chronic inflammatory disease characterized by progressive damage of diarthrodial joints, with variable extra-articular manifestations. Since RA is a disease with highly variable presentation between patients and in course of the disease within individual joints; evaluation of different aspects of the disease like (a) articular swelling, pain and stiffness; (b) extra-articular and systemic features like sub febrile temperature, weight loss and

fatigue are of paramount importance. All these parameters are complicated and this has led to large number of variables used for evaluation of disease activity, severity, extent and its outcome is of major importance in both daily practice and clinical trials.¹ Rheumatoid arthritis is considered to occur when genetic and environmental factors interact to trigger immunopathological changes and consequently an inflammatory arthritis. Multiple environmental factors including hormones, dietary factors, infections and exposure to tobacco smoke as well as gene-environment

interactions have been associated with increased risk of rheumatoid arthritis.² Mucociliary clearance is a primary defense mechanism in the human airways. The nasal mucociliary clearance (NMC) system transports the mucus layer that covers the nasal epithelium towards the nasopharynx by cilia beating at a frequency of 7-16 Hz at body temperature.³ The primary function of the NMC system is to protect the respiratory system from damage by inhaled substances. Mucociliary clearance is in part dependent on the physiological characteristics of mucus and in part on ciliary functions like beat frequency and coordination.⁴

Various factors like ageing, temperature (<10°C and >45°C), drugs like adrenaline, acetylcholine, and corticosteroids influence the duration of NMC. Mucociliary clearance can be measured both in upper and lower respiratory tracts by the measuring the rate of removal of radiolabeled particles or radiopaque discs. Also, the ciliary beat frequency can be assessed as an indicator of ciliary function.⁵ But the saccharin test described by Andersen et al. is an inexpensive, non-invasive, simple, and reproducible technique to assess the NMC.⁶ It is as efficacious as the measurement of clearance using radiolabeled particles.⁷ In fact, it has been proposed as an effective screening test to detect abnormal NMC.⁸

The aim of this study was to evaluate nasal mucociliary clearance time in patients with rheumatoid arthritis with disease duration of more than five years.

METHODS

The study was conducted in the Department of Physiology, Pt. B.D. Sharma PGIMS, Rohtak in 50 females of age group 30-50 years. Control group comprised of 25 healthy volunteer females while study group comprised of 25 rheumatoid arthritis female patients with disease duration of more than five years from rheumatology clinic of Pt. B.D. Sharma PGIMS, Rohtak.

Proven cases of RA (as per 1987 ACR criteria) were taken with disease duration of more than five years. Nasal allergy, chronic rhinitis, chronic sinusitis, ear discharge, chronic hepatic, renal and respiratory diseases were excluded.

A 0.5 mm of saccharin particle was placed on the inferior nasal turbinate 1cm from its anterior end. The test was carried out in sitting position and patient was not told about the nature of particle. The subject was instructed not to snuff, eat, drink, or swallow and to avoid coughing and sneezing if possible during the test. When they experienced the sweet taste sensation at the posterior nasopharynx the nasal mucociliary transport time was recorded in seconds. An informed consent was taken from the patients to participate in the study. The data

collected in the study was compiled and analyzed by students 't' test.

RESULTS

Rheumatoid arthritis is associated with different lung disorders which include pleural effusions, pulmonary rheumatoid nodules, bronchiectasis and lung infections. Surprisingly little attention has been given to the airways in RA. Our study analyzed mucociliary clearance by saccharin test so that it may provide grounds for suspected diagnosis of respiratory infections in RA. In our study, most affected age group was 30-35 years constituting 36% of the cases studied and most common age group for control was 36-40 years.

Twelve cases (48 %) fell in 5-10 years duration group. Ten (40%) patients fell in 11-15 years duration group, two (8%) in 16-20 years and only one patient in 26-30 years duration group. Most common joint involved was metacarpophalangeal joint and proximal interphalangeal joint, wrist joint was comparatively less involved.

In our study in right nose, the mean NMC was increased and was statistically very highly significant in rheumatoid arthritis patients (15.52 ± 4.24) in comparison to control (5.44 ± 1.29 , $p < 0.001$) as shown in Table 1.

Table 1: Comparison of mean nasal mucociliary clearance of right nose of between group I and group II.

	Group I (mean \pm SD)	Group ii (mean \pm SD)	P value
NMC	5.44 ± 1.29	15.52 ± 4.24	<0.001

In left nose, the mean NMC was increased and was statistically very highly significant in rheumatoid arthritis patients (16.28 ± 4.28) in comparison to control (5.48 ± 1.32 , $p < 0.001$) as shown in Table 2.

Table 2: Comparison of mean nasal mucociliary clearance of left nose between group I and group II.

	Group I (mean \pm SD)	Group II (mean \pm SD)	P value
NMC	5.48 ± 1.32	16.28 ± 4.28	<0.001

The results from the mucociliary clearance show that there is impairment of ciliary clearance of inhaled particles in rheumatoid arthritis patients when compared with a matched control population so chronic airway infection may occur in rheumatoid arthritis.

The results of our study also confirm that the saccharin test is a useful screening technique for measuring nasal mucociliary clearance as it is inexpensive and simple to do test.

DISCUSSION

Rheumatoid arthritis is the most common autoimmune disease characterized by chronic systemic inflammation that affects many tissues especially synovial tissue leading to joint destruction. RA related injuries can occur to other tissues, including the lung. This extra-articular tissue involvement was earlier thought of being a target of RA-related autoimmunity, or an effect of medications or secondary infections. However, emerging data has shown that the lung may play a role in the initiation of RA due to gene and environmental interactions at the mucosal surface of the lung. Pulmonary involvement is one of the most common extraarticular manifestations and the second cause of death by infection. While the joints are the predominant organs targeted by immune and inflammatory responses in RA, other tissues can be affected as well. The extra-articular involvement in RA can include cutaneous, ocular, cardiac, neurologic and hematologic manifestations. It has been hypothesized that RA-associated autoantibody generation occurs at inflamed mucosal surfaces, such as in the lung and oral mucosa.⁹ IgA is the predominant antibody of the mucosal immune system. The IgA-antibody system is very effective in binding particulates and viruses before they invade epithelial cells, and it aids in removal of these substances through the mucociliary clearance system. IgA ACPA is highly specific for RA in individuals with preclinical and early RA.¹⁰

The respiratory epithelium is lined with cilia that normally carry out an integrated and coordinated mechanism called mucociliary clearance. Mucociliary clearance is the process by which cilia transport the viscous mucus blanket of the upper airway to the gastrointestinal tract, by which the upper airway clears itself of pathogens, allergens, debris, and toxins.¹¹

Potentially harmful substances get trapped in the mucus layer lining the airways, and subsequently, the synchronized movement of the cilia propels the mucus to the pharynx where it will be swallowed. This mechanism can be hampered either by conditions affecting the constitution of the mucus (such as cystic fibrosis, chronic obstructive pulmonary disease, or asthma) or by conditions directly affecting the movement of the cilia.

Mucociliary clearance is a key defense mechanism in human upper and lower airways and its impairment both acquired and genetically determined predisposes to chronic infection of the nose, paranasal sinuses and respiratory tree. There is evidence that mucociliary clearance that occurs in the trachea and main bronchi at a similar rate as in the nose thus its measurement can be used as a screening test. Mucociliary clearance depends on two principal components, the physiochemical qualities and the quantity of mucus and the properties of cilia that propel it; these can be affected by the disease.¹²

Techniques to measure clearance time in trachea and bronchi are time consuming, cumbersome and expensive, measurement of NMC using saccharin test serves as a good alternative and is representative of clearance in trachea and bronchi.¹³

Prolonged NMC causes stagnation of mucus and impaired mucus drainage thus can predispose to sinonasal and middle ear infections. Further, impaired drainage causes increased viscosity, altered levels of complements, lysozymes, and immunoglobulins resulting in poor immunological protection, increased incidence of nasal allergies and chronic rhinosinusitis.¹⁴ Prolonged clearance observed in our study may be due to slowed ciliary beat frequency or reduction in number of cilia and changes in viscoelastic properties of mucus. If ciliary motility is defective mucus transport is absent thus can lead to chronic sinusitis, recurrent lung infections and bronchiectasis. Our study shows the important role of mucociliary clearance in the health of sinonasal cavities.

CONCLUSION

From the present study, it can be concluded that impairment of mucociliary clearance can occur in rheumatoid arthritis and it seems to be the result of qualitative and quantitative alterations in respiratory secretions. Clinicians must follow-up these patients more closely for sinonasal and middle ear infections.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: Not required

REFERENCES

1. Silman AJ, Pearson JE. Epidemiology and genetics of rheumatoid arthritis. *Arthritis research and therapy*. 2002 May 9;4(3):S265.
2. Karlson EW, Deane K. Environmental and gene-environment interactions and risk of rheumatoid arthritis. *Rheumatic Disease Clinics of North America*. 2012;38(2):405-26.
3. Pandya VK, Tiwari RS. Nasal mucociliary clearance in health and disease. *Ind J Oto Head and Neck Surg*. 2006;58(4):332-4.
4. Robinson M, Bye PT. Mucociliary clearance in cystic fibrosis. *Pediatr Pulmonol*. 2002;33:293-306.
5. Baby MK, Muthu PK, Johnson P, Kannan S. Effect of cigarette smoking on nasal mucociliary clearance: A comparative analysis using saccharin test. *Lung India*. 2014;31:39-42.
6. Andersen I, Proctor DF. Measurement of nasal mucociliary clearance. *Eur J Respir Dis Suppl*. 1983;127:37-40.
7. Yergin BM, Saketkhoo K, Michaelson ED, Serafini SM, Kovitz K, Sackner MA. A roentgenographic method for measuring nasal mucous velocity. *J Appl Physiol*. 1978;44:964-8.

8. Andersen I, Camner P, Jensen PL, Philipson K, Proctor DF. Nasal clearance in monozygotic twins. *Am Rev Respir Dis.* 1974;110:301-5.
9. Demoruelle MK, Deane KD, Holers VM. When and where does inflammation begin in rheumatoid arthritis? *Curr Opin Rheumatol.* 2014;26:64-71.
10. Svard A, Kastbom A, Soderlin MK, Reckner-Olsson A, Skogh T. A comparison between IgG and IgA class antibodies to cyclic citrullinated peptides and to modified citrullinated vimentin in early rheumatoid arthritis and very early arthritis. *J Rheumatol.* 2011;38:1265-72.
11. Gudis DA, Cohen NA. Cilia dysfunction. *Otolaryngol Clin North Am.* 2010;433:461-72.
12. Corbo GM, Foresi A, Bonfitto P, Mugnano A, Agabiti N, Cole PJ. Measurement of nasal mucociliary clearance. *Arch Dis Childhood.* 1989;64:546-50.
13. Andersen I, Camner P, Jensen PL, Philipson K, Proctor DF. A comparison of nasal and tracheobronchial clearance. *Arch Environ Health.* 1974;29:290-3.
14. Mezey RJ, Cohn MA, Fernandez RJ, Januszkiewicz AJ, Wanner A. Mucociliary transport in allergic patients with antigen-induced bronchospasm. *Am Review Respir Dis.* 1978;118:677-84.

Cite this article as: Deswal S, Yadav J, Deswal M, Singh H. Evaluation of nasal mucociliary clearance in rheumatoid arthritis: a comparative analysis using saccharin test. *Int J Res Med Sci* 2017;5:5026-9.