This is an Accepted Manuscript for *The Journal of Laryngology & Otology*
DOI: 10.1017/S0022215122001219

QUAIL EGG HOMOGENATE WITH ZINC AS ADJUNCTIVE THERAPY IN SEASONAL ALLERGIC RHINITIS: A RANDOMIZED CONTROLLED TRIAL

Author 1: Claudio Andaloro, MD

Author 1: Unit of Otorhinolaryngology, Department of Medical Sciences Surgical and Advanced Technologies "GF Ingrassia", University of Catania, Catania, Italy.

Author 2: Alberto Maria Saibene, MD, MA

Author 2: Otolaryngology Unit; ASST Santi Paolo e Carlo, Department of Health Sciences, Università degli Studi di Milano, Milan, Italy

Author 3: Ignazio La Mantia, PhD

Author 3: Unit of Otorhinolaryngology, Department of Medical Sciences Surgical and Advanced Technologies "GF Ingrassia", University of Catania, Catania, Italy.

Author for correspondence: Dr. Claudio Andaloro, Unit of Otorhinolaryngology, Department of Medical Sciences Surgical and Advanced Technologies "GF Ingrassia", University of Catania, Catania, Italy.

Email: cla.anda@gmail.com

Fax: +39 0916 763 409

Abstract

Objective. Since most available treatments manage seasonal allergic rhinitis (SAR) show some side effects without reducing recurrences, natural anti-allergic products could represent an interesting treatment addition. We aimed to study the efficacy and tolerance of quail egg as adjunctive therapy in SAR.

Methods. In a CONSORT compliant framework, patients with SAR were prospectively randomized to receive mometasone nasal spray for four weeks (M) or the same topic corticosteroid therapy plus oral commercially available quail egg and zinc tablets (M+N).

Results. Forty patients were enrolled. The M+N group showed a greater reduction in nasal itching, sneezing, and total nasal symptom scores than the M group. A higher proportion of participants in the M+N group had good rhinitis control than in the M group, with no need for rescue medications.

Conclusion. Despite the need for further larger study, quail egg preliminary appears as an effective adjunct to topical steroid therapy in SAR.

Key Words: Seasonal allergic rhinitis; Quail; Anti-allergic agents; Mometasone furoate

INTRODUCTION

Seasonal allergic rhinitis (SAR; or hay fever), an antigen-mediated inflammation of the nasal mucosa that may extend into the paranasal sinuses due to an allergic reaction to allergens as pollens, is the most common atopic disorder. Its prevalence ranges from 10 to 40% of all adults, with higher rates in Western countries.[1,2] Its prevalence has had nearly a two-fold increase in the last twenty years, with more significant rises in formerly low-prevalent countries.[2,3] This increase is paralleled by an increase in comorbidities such as asthma.[4] SAR is featured by a runny nose, congestion, sneezing, and sinus pressure. SAR is usually a non-life-threatening issue but it is considered a major chronic respiratory disorder due to its high incidence and impact on the quality of life, healthcare costs, mood, social functioning, work/school performance, and sleep.[2,5-7]

SAR is due to a type I hypersensitivity following the release of the granule-stored mediators such as proteases, histamine, lipid mediators, and cytokines from mast cells.[8] These mast-cell mediators can sustain and/or amplify the inflammation by supporting the inflow of inflammatory cells, increasing tissue inflammation. The only long-lasting treatment, i.e., immunotherapy, has variable efficacy and duration, therefore other treatments are frequently utilized in order to control symptoms. First-line management is usually based on the identification and avoidance of the causing allergens, coupled with decongestants and second-generation antihistamines drug use. Second-line interventions consist of anti-leukotrienes, steroids, and anticholinergics. Immunotherapy still represents a third-line treatment, mostly because of its cost. It is well-known that first-generation antihistamines may cause side effects like drowsiness, dizziness, headache, loss of appetite, stomach upset, vision changes, irritability, dry mouth, and nose.[9,10] Second-generation antihistamines have poor efficacy in the management of more severe cases[9] and in treating perennial rhinitis, because symptoms, predominantly nasal obstruction, are not histamine-mediated.[11,12] Topical nasal corticosteroids are commonly prescribed; however, the safety of these compounds remains controversial. Main

https://doi.org/10.1017/S0022215122001219 Published online by Cambridge University Press

concerns derive from dose-related systemic adverse effects associated with long-term treatments (e.g., adrenocortical function suppression, growth, and bone metabolism alterations[9,13]). Since commonly employed drugs not only may induce known adverse reactions but do not impact on symptoms recurrences, natural antiallergic products could represent a further useful tool in antiallergic treatment.

Prior research suggests that quail egg (QE) has a high protein content with antiallergic, anti-inflammatory, and anti-cancer activities.[14-18] Several studies suggested that daily oral QE administration may weaken allergic asthma and rhinitis symptoms.[15,16] Furthermore, it has been shown that QE has therapeutic potential in modulating the inflammatory response and reducing the manifestations of food allergy-induced eosinophilic esophagitis disease.[14] QE has an antiallergic action via inhibiting the activation of mast cells. As histamine, tryptase, Th2, and pro-inflammatory-related cytokines are related to several allergic and inflammatory disorders, downregulating their mast cells secretion could prove useful. In this randomized controlled trial, we aimed to compare the efficacy and immediate tolerance of oral quail eggs as a supplement of nasal mometasone spray in a randomized controlled trial setting.

MATERIALS AND METHODS

A CONSORT compliant, open-label, randomized controlled trial with a parallel-group design was conducted to evaluate the efficacy and immediate tolerance of a one-month treatment regime with a commercially available zinc and QE dietary supplement combined with Mometasone nasal spray in improving SAR symptoms. The study was implemented from February to September 2019 at the University of Catania. The CONSORT checklist for randomized clinical studies is available in Supplementary File 1.

Patients were eligible to participate if the following inclusion criteria were met: a) age ≥18 years old; b) with a recent diagnosis of mild to severe SAR to the most common inhalant allergens prevalent in the geographic area in which the study was carried out (*Lolium perenne, Phleum*

https://doi.org/10.1017/S0022215122001219 Published online by Cambridge University Press

pratense, Secale cereale, Holcus lanatus, Parietaria Judaica, Artemisia vulgaris, Olea europaea, and *Alternaria tenuis*; and c) no ongoing treatment for SAR. Diagnosis and severity of SAR are based on the Allergic Rhinitis and its Impact on Asthma (ARIA) guidelines, in combination with positive skin test reactions to suspected allergens and a positive determination of allergen-specific serum IgE levels (ImmunoCAP, Pharmacia Diagnostics AB, Uppsala, Sweden), specific IgE values of ≥0.35 kU/L were considered indicative of aeroallergen sensitization. All patients underwent the same common inhalant allergen panel evaluation composed of 12 items. An allergen schedule specific for Southern Italy can be seen in Supplementary File 2.

Exclusion criteria were:

- any other chronic medical condition (including uncontrolled asthma)
- pregnancy
- concomitant respiratory tract infection
- administration of systemic or topical antihistamine, leukotriene receptor antagonist, and/or decongestant drugs within the week before the study participation
- systemic or topical corticosteroid use within the month before the study participation
- known sensitivities to any of the ingredients of the study product.

The researchers employed a convenience sampling design to select study participants. Patients who satisfied the inclusion/exclusion criteria were invited to participate in the study. Due to the lack of previously published studies comparing the two treatments of interest that could be used for *a priori* sample size computation, and the limited resources available to the researchers, the attained statistical power was examined instead, given a finite sample of 20 patients for each treatment arm. Post-hoc analysis revealed that the study achieved 61% power in detecting a significant difference in the mean change in Total Nasal Symptom Score (TNSS) between the two groups based on the following parameters: a) effect size of 0.73 (M group: 2.95 ± 1.73, M+N group 4.50 ± 2.44), b) alpha equal to 0.05, and c) sample size of 40 (20 for each group). Eligible patients were invited and were referred to the primary investigator for study procedure orientation and informed consent

https://doi.org/10.1017/S0022215122001219 Published online by Cambridge University Press

administration. A statistician not related to this study generated the allocation schedule before the start of the study by using a statistical computing web programming tool (available at www.graphpad.com/quickcalcs). A simple randomization technique was used to allocate the patients to two groups in a 1:1 ratio. The allocation schedule was concealed from study researchers until study termination.

Patients were assigned a number sequentially according to their study entry by the primary investigator. Patients received the treatment assigned to their number based on the allocation schedule. G*Power 3.1.9.2 software was used for power analysis.

A CONSORT compliant diagram with patient allocation and analysis is available in Supplmentary File 3. Patients were randomly allocated into two groups—the M group and M+N group. The M group received 100 mcg mometasone nasal spray (Nasonex, Merck, Kenilworth, NJ, US) and were instructed to administer two sprays in each nostril once daily for four weeks. Patients assigned to the M+N group were instructed to take Narivent (DMG, Rome, Italy) oral soluble tablets, which contain quail egg homogenate and zinc (average values for 2 tablets consist of quail egg powder 84 mg and zinc 1.5 mg), twice a day, morning and evening, preferably between meals, for four weeks in addition to the Mometasone nasal spray. Patients were also informed that the tablets should be chewed or sucked slowly until they are completely dissolved in the mouth. Patients were allowed to use cetirizine 5 mg (once daily) as rescue medication during the treatment period.

At their first visit, the primary investigator obtained the following baseline demographic and clinical data: age, sex, BMI, smoking status, rhinitis type, and rhinitis severity based on the Allergic Rhinitis and its Impact on Asthma (ARIA) guidelines.[2] Also, the following measures were obtained at baseline and at the end-of-study visit to assess efficacy:

- Total Nasal Symptom Score (TNSS) included four parameters related to symptoms (rhinorrhea, nasal congestion, nasal itching, sneezing). The intensity was calculated by total and individual nasal symptoms score using a numerical score scale (0 – no symptoms, 3 – severe).[19]

https://doi.org/10.1017/S0022215122001219 Published online by Cambridge University Press

- Rhinitis Control Assessment Test (RCAT) Self-administered instrument for evaluating symptom control in patients with rhinitis. 5-point Likert scale ("never" to "extremely often"), scores range from 6 to 30, with scores < 21 indicating bad rhinitis symptom control.[20]

- Total Nasal airflow resistance (right+left) ($Pa/cm^3/s$) were measured, using an active anterior rhinomanometry (Rhino Pocket ED 200; Euro Clinic, Castel Bolognese, Italy) by using a standard protocol. Total nasal airflow resistance reflects the resistance of both sides of the nasal cavity. Normal values range is 0.10-0.40 $Pa/cm^3/s$.[21]

- Total plasma IgE (IU/mL)

Furthermore, at each visit patients underwent a general otolaryngological examination and a flexible nasal endoscopy.

Patients were asked to return one month after treatment initiation to assess the study outcomes. The use of cetirizine rescue doses, as well as the presence of adverse events, were recorded at follow-up.

This study was conducted in accordance with the Declaration of Helsinki and the note for guidance on good clinical practice (ICH-GCP). The study was approved by the Ethics Committee of the School of Medicine - ASP 3 Catania (id: 077/19). All patients were given written informed consent before their enrolment. Moreover, the trial was registered by the German Clinical Trials Register with the following code: DRKS00023981.

Data were encoded in MS Excel by the researcher. Stata MP version 14 software was used for data processing and analysis. Continuous data were presented as mean/standard deviation (SD) or median/interquartile range (IQR) depending on data distribution. Shapiro Wilk's test was used to assess data normality. Categorical data were presented as frequency and percentage. Independent t-test or Mann-Whitney U test was used to analyse continuous variables. Fisher's exact test was used to analyse categorical variables. P-values ≤ 0.05 were considered statistically significant. The intention-to-treat principle was implemented.

RESULTS

https://doi.org/10.1017/S0022215122001219 Published online by Cambridge University Press

Forty patients were included in the study as planned and 20 patients were randomized to each treatment arm (see Supplementary File 3). Table 1 compares the demographic and clinical profile of patients by treatment group. The median age of all patients was 38.5 years (range 19-51 years). Most patients were males (60%). There was no significant difference observed between the two groups in terms of median age, sex, median BMI, smoking status, rhinitis type, rhinitis severity, nasal symptom score, RCAT, total nasal airflow resistance, and total plasma IgE (P-value >0.05).

Table 2 compares the mean change in the nasal symptom scores between the two groups. The mean reduction in rhinorrhoea, nasal itching, and sneezing scores was found to be higher in the M+N group, however, statistical significance was only observed in sneezing and nasal itching scores. The mean change in total nasal symptom score was also found to be significantly higher in the M+N group.

Among the secondary outcomes, only the change in RCAT score was significantly different between the two groups. A higher proportion of participants in the M+N group had good rhinitis control and normal total nasal airflow resistance as compared to those in the M group, but the results were statistically significant only in the first case. None of the participants in the M+N group required rescue medication (cetirizine). Only 2 patients (10%) for each group developed adverse events —2 patients in the M+N group had nasal dryness, one patient in the M group developed nasal dryness and one had epistaxis. No significant difference in the proportion of patients who developed adverse events was observed.

All patients completed the intended one-month treatment regime and no patients were lost to follow-up.

DISCUSSION

In our randomized clinical trial, we found a significantly higher mean reduction in nasal itching and sneezing scores and mean change in total nasal symptom score in the M+N group. Among the secondary outcomes, the change in the RCAT score was significantly different between the two

https://doi.org/10.1017/S0022215122001219 Published online by Cambridge University Press

groups. A significantly higher proportion of participants in the M+N group had a good rhinitis control as compared to those in the M group.

In line with our findings, two previous clinical trials[16,22] supported the efficacy and safety of a quail eggs dietary supplement for the symptomatic treatment of SAR symptoms. In contrast with those results, our trial revealed a significant improvement in sneezing scores following administration of the drug and not in nasal congestion. This is most likely due to the fact that we used nasal steroids in both groups. There is raising evidence that intranasal corticosteroids provide a better effect than antihistamines on nasal blockage,[23] and this would explain the lack of difference in nasal blockage between the two groups. This is also supported by the absence of significant difference as well in nasal airflow resistance. The use of QE as an adjunct to an already commonly employed and effective therapy such as topical mometasone allowed our study to give more relevance to the role of QE as an adjunct to baseline therapy, in contrast with prior studies on this subject.

Despite QE not appearing very effective in the obstructive symptoms, it was indeed effective in terms of sneezing and itching scores. This could be due to its potential in inhibiting the cascade of immune-related allergic responses and blocking allergens before they can activate the immune cells. In contrast, common over-the-counter medications such as antihistamines block the activity of histamine after it has been released during an allergic attack.[22,24]

The use of natural dietary supplements, with a lower adverse events risks profile and with no intrinsic contraindications other than known component allergy, might prove a useful integration for symptomatic management of SAR.[24] QE consists mainly of water, proteins especially ovomucoids and ovoinhibitors, fats, minerals, and carbohydrates.[25] In vitro data showed that these proteins may act as inhibitors of serine proteases[17,26] which present in some outdoor and indoor antigens causing tissue injury and stimulate IgE-mediated allergic response. Thus, QE seems to attenuate the periodic manifestations of an allergic reaction.[16,27] Besides, toxicological research including an acute and repeated oral administration on rats as well as in vitro studies demonstrated good tolerability of QE without genotoxic or mutagenic problems.[18] Another research demonstrated that oral QE succeeded

https://doi.org/10.1017/S0022215122001219 Published online by Cambridge University Press

in reducing immune reactions and manifestations of peanut-sensitized mice with eosinophilic esophagitis-like disorder, confirming the apparent antiallergic role of QE.[28] It was observed that farmers having quails had fewer allergic manifestations than the general population in the same area.[15] Of note, cases suffering from outdoor and indoor allergens were given QE powder or placebo. It was shown that consumption of QE resulted in symptoms relief with good tolerability.[18] Not only preclinical studies but also some clinical trials investigated the efficacy and safety of QE. Benichou et al. found out good symptomatic relief with no side effects in cases having induced manifestations of SAR.[16] Syrigou and co-workers[22] found improved nasal flow and patency in individuals with active symptoms, as documented by the statistically suggestive increase of peak nasal inspiratory flow (PNIF) in comparison to pre-interventional values. A significantly reduced visual analogical scale (VAS) score has been detected for all AR-associated symptoms, which appeared more for nasal than ocular symptoms. It is worth mentioning that both PNIF and VAS improvements had statistical significance within 15 to 30 minutes from QE administration, except for watery eyes which took longer to respond. QE led to better nasal patency and breathing than placebo.[16]

Zinc, a pivotal mineral in QE, has a well-established role in several physiological processes, due to its immunoregulatory, anti-inflammatory, and antioxidant functions.[29] A suggested anti-inflammatory mechanism of zinc includes suppression of the interaction between a cell surface antigen of neutrophils, leucocyte-related antigen I, and intracellular adhesion molecule I, another cell surface antigen which is expressed not only by inflammatory cells but also by the nasal epithelium and regulates the inflammatory response in SAR.[29-31] Oral zinc supplement was detected to inhibit inflammation of the epithelial airway in animals,[32] to enhance lung functions in individuals with cystic fibrosis,[31] to benefit cases with atopic asthma, common cold, a lower respiratory tract infection, pneumonia, and tuberculosis and to reduce respiratory tract infection rates in children.[33]

https://doi.org/10.1017/S0022215122001219 Published online by Cambridge University Press

It was observed that QE albumen played the most effective role as compared to QE yolk in modulating mast cells degranulation by suppressing the release of β-hexosaminidase, histamine, tryptase, and pro-inflammatory cytokines and upregulating the release of IL-10. It was shown that the lowest levels of QE albumen already had a significant inhibitory effect on modulating these mediators. Even though QE yolk also showed a significant therapeutic effect to modulate these mediators despite being not as strong as QE albumen. However, QE yolk showed a greater significant inhibition effect as compared to QE albumen on modulating the cytokines. The augmentation of Th2 cytokines in a higher concentration of QE was not surprising as it is largely known that QE itself contained many described egg allergens which also may act on immune pathway regulation to provide benefit in the occurrence of allergy reactions. Besides, the effective effect of QE yolk on modulating Th2 cytokines likely due to its high nutrient contents which likely also play an important role as anti-allergic agents.[34] The antiallergic inflammatory activity and mast cell stabilizing role of QE appears to be due to the inhibition of allergic mediators secretion, depletion of endoplasmic reticulum Ca2+ store, and intracellular Ca2+ influx generation through the inhibition of PAR-2 downstream signalling transduction pathway.[14]

Our study has several intrinsic design limitations. First and foremost, its pilot nature led to a brief effectiveness evaluation period. Although one month of therapy was enough to suggest a superiority of QE/zinc supplement versus mometasone alone, longer study periods are required to assess long-term positive and negative side effects. Secondly, the open-label design didn't allow us to rule out the possible placebo effect related to the oral tablets supplementation. As the greater symptoms improvement in the M+N group is indeed marginal, gaining insight on the possible placebo effect induced by our dietary supplement is pivotal in order to gain definitive information on its potential. This potential bias needs to be addressed in future studies. Again, the small sample size, coupled with the short study period, didn't allow us to draw solid conclusions on the safety profile of QE, but only gain some insight on its immediate tolerance profile. This is especially true if we aim to put potential side effects in context with allergies to other species eggs (such hen) which have not

https://doi.org/10.1017/S0022215122001219 Published online by Cambridge University Press

been explored in the present study population. Furthermore, we're unable to define patients subgroups based on specifc IgE levels as they were not evaluated in our patient pool. It is interesting – and potentially a source of bias – that the median age in our study is rather high, probably as a consequence of the specific profile of patients usually accessing our outpatient department for second or third-level opinion in uncontrolled rhinitis. Undoubtedly such peculiarity must be taken into account when weighting the results of our study. Last, the compound nature of the oral supplement given to patients didn't allow us to separate the effects of QE and zinc, which may have acted synergically. A further minor point is the lack of specific laboratory tests which might have helped to shed more light on the pharmacological effects of the oral supplement, a limitation we plan to overcome in future larger studies. Nevertheless, given the lack of better-designed and more powerful studies comparing QE supplementation of topic steroids, the briefly described limitations do not hamper the overall validity of the study. Nevertheless, we are aware that, in order to definitely prove the role of QE in allergic rhinitis, these shortcomings need to be addressed in larger and longer placebo-controlled trials.

CONCLUSION

Our clinical trial preliminary shows that the use of quail eggs as an add-on therapy to intranasal steroids might have the potential to become an effective and safe adjunct to steroids in SAR management. The use of such natural dietary supplements, with their encouraging risk profile, might represent a further advancement in SAR management. Our preliminary results on QE are encouraging and call for further, larger, and possibly placebo-controlled studies. Furthermore, future studies delving into the mechanisms of action of active ingredients of QE are required to identify its therapeutic potential and antiallergic effects and might represent the first step in developing studies comparing QE - or other natural dietary supplements - against topical steroid therapy and not only as an adjunct.

https://doi.org/10.1017/S0022215122001219 Published online by Cambridge University Press

Acknowledgement. None

Financial Support: This research received no specific grant from any funding agency, commercial or not-for-profit sectors

Competing interests. None declared

REFERENCES

1. Katelaris CH, Lee BW, Potter PC, Maspero JF, Cingi C, Lopatin A, et al. Prevalence and diversity of allergic rhinitis in regions of the world beyond Europe and North America. Clin Exp Allergy 2012;42:186-207

2. Brożek JL, Bousquet J, Agache I, Agarwal A, Bachert C, Bosnic-Anticevich S, et al. Allergic Rhinitis and its Impact on Asthma (ARIA) guidelines-2016 revision. J Allergy Clin Immunol 2017;140:950-8

3. Schwindt CD, Settipane R. Allergic rhinitis (AR) is now estimated to affect some 1.4 billion people globally and continues to be on the rise. Editorial. Am J Rhinol Allergy 2012;26 Suppl 1:S1

4. Lunn M, Craig T. Rhinitis and sleep. Sleep Med Rev 2011;15:293-9

5. Zuberbier T, Lötvall J, Simoens S, Subramanian S, Church MK. Economic burden of inadequate management of allergic diseases in the European Union: a GA(2) LEN review. Allergy 2014;69:1275-9

6. Yoo KH, Ahn HR, Park JK, Kim JW, Nam GH, Hong SK, et al. Burden of Respiratory Disease in Korea: An Observational Study on Allergic Rhinitis, Asthma, COPD, and Rhinosinusitis. Allergy Asthma Immunol Res 2016;8:527-34

7. Sardana N, Craig TJ. Congestion and sleep impairment in allergic rhinitis. Asian Pac J Allergy Immunol 2011;29:297-306

8. Theoharides TC, Kalogeromitros D. The critical role of mast cells in allergy and inflammation. Ann N Y Acad Sci 2006;1088:78-99

9. Baena-Cagnani CE. Safety and tolerability of treatments for allergic rhinitis in children. Drug Saf 2004;27:883-98

10. Hardjojo A, Shek LP, van Bever HP, Lee BW. Rhinitis in children less than 6 years of age: current knowledge and challenges [published correction appears in Asia Pac Allergy. 2012 Jan;2(1):90. Hadjojo, Antony [corrected to Hardjojo, Antony]]. Asia Pac Allergy 2011;1:115-22

11. Greiner AN, Hellings PW, Rotiroti G, Scadding GK. Allergic rhinitis. Lancet 2011;378:2112-22

12. Turner PJ, Kemp AS. Allergic rhinitis in children. J Paediatr Child Health 2012;48:302-10

13. Al Sayyad JJ, Fedorowicz Z, Alhashimi D, Jamal A. Topical nasal steroids for intermittent and persistent allergic rhinitis in children. Cochrane Database Syst Rev 2007;2007(1):CD003163

14. Knoops L, Louahed J, Van Snick J, Renauld J-C. IL-9 promotes but is not necessary for systemic anaphylaxis. J Immunol 2005;175:335-41

15. Truffier J. Approche therapeutique de la maladie allergique par ingestion d'oeufs de caille. La clinique 1978;22:2-4

16. Benichou AC, Armanet M, Bussière A, Chevreau N, Cardot JM, Tétard J. A proprietary blend of quail egg for the attenuation of nasal provocation with a standardized allergenic challenge: a randomized, double-blind, placebo-controlled study. Food Sci Nutr 2014;2:655-63

17. Feeney RE, Means GE, Bigler JC. Inhibition of human trypsin, plasmin, and thrombin by naturally occurring inhibitors of proteolytic enzymes. J Biol Chem 1969;244:1957-60

18. Bruttman G. Ovix. Quail egg homogenate: a clinical evaluation. La Med Biol 1995;2:25-9

19. Ellis AK, Soliman M, Steacy L, Boulay M, Boulet L-, Keith PK, et al. The Allergic Rhinitis - Clinical Investigator Collaborative (AR-CIC): nasal allergen challenge protocol optimization for studying AR pathophysiology and evaluating novel therapies. Allergy Asthma Clin Immunol 2015;11(1):16

20. Nathan RA, Dalal AA, Stanford RH, Meltzer EO, Schatz M, Derebery J, et al. Qualitative Development of the Rhinitis Control Assessment Test (RCAT), an Instrument for Evaluating Rhinitis Symptom Control. Patient 2010;3:91-9

21. Ottaviano G, Fokkens WJ. Measurements of nasal airflow and patency: a critical review with emphasis on the use of peak nasal inspiratory flow in daily practice. Allergy 2016;71:162-74

22. Syrigou E, Psarros F, Makris M, Grapsa D, Syrigos K. Efficacy of a Quail Eggs-Based Dietary Supplement for Allergic Rhinitis: Results of a Single-Arm Trial. J Diet Suppl 2021;18:17-30

23. Mygind N, Dahl R, Nielsen LP, Hilberg O, Bjerkex T. Effect of corticosteroids on nasal blockage in rhinitis measured by objective methods. Allergy 1997;52:39-44

24. Aaronson DW. Side effects of rhinitis medications. J Allergy Clin Immunol 1998;101:S379-82

25. Prelipcean A, Prelipcean A, Teuşan V. Investigations on the structure, chemical composition and caloricity of the quail eggs, deposited at the plateau phase of the laying period. Lucrari Stiintifice–Seria Zootehnie 2012;57:113-20

26. Vergnaud S, Bruttmann G, Louwagie M, Morel F. Effetto inibitorio dell'ovomucoide di uovo di quaglia giapponese sull'attività di tripsina ed elastasi umane. La Med Biol 2007;2:5-13

27. Widmer F, Hayes PJ, Whittaker RG, Kumar R. Substrate preference profiles of proteases released by allergenic pollens. Clin Exp Allergy 2000;30:571-6

28. Lianto P, Han S, Li X, Ogutu FO, Zhang Y, Fan Z, et al. Quail egg homogenate alleviates food allergy induced eosinophilic esophagitis like disease through modulating PAR-2 transduction pathway in peanut sensitized mice. Sci Rep 2018;8:1049

29. Zalewski PD, Truong-Tran AQ, Grosser D, Jayaram L, Murgia C, Ruffin RE. Zinc metabolism in airway epithelium and airway inflammation: basic mechanisms and clinical targets. A review. Pharmacol Ther 2005;105:127-49

30. Novick SG, Godfrey JC, Pollack RL, Wilder H. Zinc-induced suppression of inflammation in the respiratory tract, caused by infection with human rhinovirus and other irritants. Med Hypotheses 1997;49:347-57

31. Demoly P, Sahla M, Campbell AM, Bousquet J, Crampette L. ICAM-1 expression in upper respiratory mucosa is differentially related to eosinophil and neutrophil inflammation according to the allergic status. Clin Exp Allergy 1998;28:731-8

32. Lu H, Xin Y, Tang Y, Shao G. Zinc suppressed the airway inflammation in asthmatic rats: effects of zinc on generation of eotaxin, MCP-1, IL-8, IL-4, and IFN-γ. Biol Trace Elem Res 2012;150:314-21

33. Mohamed NA, Rushdy M, Abdel-Rehim ASM. The immunomodulatory role of zinc in asthmatic patients. Cytokine 2018;110:301-5

34. Tolik D, Poławska E, Charuta A, Nowaczewski S, Cooper R. Characteristics of egg parts, chemical composition and nutritive value of Japanese quail eggs--a review. Folia Biol (Krakow) 2014;62:287-92

Bullet Point Summary

- Most available treatments manage seasonal allergic rhinitis (SAR) with some side effects and without reducing recurrences, natural anti-allergic products could represent an interesting addition for SAR management.

- Quail egg (QE) has a high protein content with antiallergic and anti-inflammatory activities which may weaken allergic asthma and rhinitis symptoms.

- The antiallergic inflammatory activity of QE appears to be due to the inhibitory effects on mast cells degranulation by suppressing PAR-2 downstream signalling transduction pathway.

- In this study, the use of QE as an add-on therapy to intranasal steroids has the potential to become an effective and safe adjunct to steroids alone in SAR management.

https://doi.org/10.1017/S0022215122001219 Published online by Cambridge University Press

Table 1. Baseline demographic and clinical profile of patients (n=40)

Characteristics	**M group (n=20) n (%)**	**M+N group (n=20) n (%)**	**P-value**
Age (in years), median	38.50 [IQR: 31.50-43]	39 [IQR: 31.50-43]	0.8922[a]
Sex			
Male	13 (65)	11 (55)	0.748[b]
Female	7 (35)	9 (45)	
BMI (in kg/m^2)	29 [IQR: 25.50-32]	28 [IQR: 25.50-31]	0.7030[a]
Smoking status			
Yes	4 (20)	2 (10)	0.661[b]
No	16 (80)	18 (90)	
Rhinitis type			
Persistent	12 (60)	14 (70)	0.741[b]
Intermittent	8 (40)	6 (30)	
Rhinitis severity			
Mild	11 (55)	9 (45)	0.752[b]

https://doi.org/10.1017/S0022215122001219 Published online by Cambridge University Press

Moderate	9 (45)	11 (55)	
Nasal symptoms at baseline			
Rhinorrhea score, median	2 [IQR: 1-2]	2 [IQR: 2-2]	0.2353[a]
Nasal congestion score, median	2 [IQR: 1-2]	2 [IQR: 1-3]	0.8190[a]
Nasal itching score, median	2 [IQR: 1-3]	2 [IQR: 1-2.5]	0.3751[a]
Sneezing score, median	2 [IQR: 1-2]	2 [IQR: 1-2]	0.8955[a]
Total Nasal Symptom Score	6 [IQR: 5.5-9.5]	8 [IQR: 5.5-9]	0.9341[a]
RCAT at baseline, median	20 [IQR: 14-21]	19 [IQR: 14-21]	0.8699[a]
Good rhinitis control	6 (30)	5 (25)	0.9610[b]
Bad rhinitis control	14 (70)	15 (75)	
Total nasal airflow resistance, median	0.33 [IQR: 0.28-0.44]	0.39 [IQR: 0.33-0.45]	0.1294[a]
Normal	15 (75)	11 (55)	0.320 [b]

https://doi.org/10.1017/S0022215122001219 Published online by Cambridge University Press

Abnormal	5 (25)	9 (45)	
Total plasma IgE (IU/ml), median	735.25 [IQR: 692.8-840.4]	699.8 [IQR: 670.5-755.95]	0.1165[a]

[a]*Mann Whitney U test was used;* [b]*Fisher's exact test was used*

Table 2. Mean change in nasal symptom score by treatment group (n=40)

Outcomes	**M group (n=20) Mean ± SD**	**M+N group (n=20) Mean ± SD**	**P-value[a]**
Nasal symptoms			
Rhinorrhea score	0.6 ± 0.5	1.05 ± 0.89	0.0557
Nasal congestion score	1.5 ± 0.76	1.35 ± 1.04	0.6057
Nasal itching score	0.3 ± 0.86	0.9 ± 1.02	0.042*
Sneezing score	0.55 ± 0.69	1.2 ± 1.11	0.0314*
Total nasal symptom score	2.95 ± 1.73	4.5 ± 2.44	0.0259*

https://doi.org/10.1017/S0022215122001219 Published online by Cambridge University Press

[a]*Independent t-test was used.*

Table 3. Secondary outcomes by treatment group (n=40).

Outcomes	**M group (n=20) Mean ± SD**	**M+N group (n=20) Mean ± SD**	**P-value**[a]
Change in RCAT, median	2 [IQR: 0-3.5]	5 [IQR: 1.5-7]	0.0478[a]
Good rhinitis control	8 (40)	13 (65)	0.049[b]
Bad rhinitis control	12 (60)	7 (35)	
Total nasal airflow resistance			
Normal	15 (75)	17 (85)	0.295[b]
Abnormal	5 (25)	3 (15)	
Change in total plasma IgE (IU/ml) [Baseline score – Follow-up score]	0 [IQR: -0.60-1.20]	0 [IQR: -0.10-8.50]	0.47[b]
Rescue medication use (cetirizine)			
Yes	3 (15)	0	0.231[b]
No	17 (85)	20 (100)	

https://doi.org/10.1017/S0022215122001219 Published online by Cambridge University Press

Adverse events			
Yes	2 (10)	2 (10)	1[b]
No	18 (90)	18 (90)	

[a]Mann-Whitney U test was used; [b]Fisher's exact test was used.

https://doi.org/10.1017/S0022215122001219 Published online by Cambridge University Press