

BRIEF COMMUNICATION

Salt chamber treatment is ineffective in treating eosinophilic inflammation in asthma

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To cite this article: Sandell J, Hedman J, Saarinen K, Haahtela T. Salt chamber treatment is ineffective in treating eosinophilic inflammation in asthma. *Allergy* 2012; DOI: 10.1111/all.12061.

Keywords

asthma; eosinophils; halotherapy; sputum.

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The Ethics Committee of South Karelia Central Hospital approved the study protocol, and all patients gave their written consent prior to the commencement of the study.

Accepted for publication 27 September 2012

DOI:10.1111/all.12061

Edited by: Michael Wechsier

Abstract

Background: We have shown that salt chamber treatment reduces airway hyper-responsiveness as an add-on therapy in adult asthmatics on inhaled corticosteroids.

Methods: We assessed whether this effect is due to the suppression of eosinophilic airway inflammation. Thirty-nine adult asthmatics on inhaled corticosteroids were randomized to receive active salt chamber treatment with low-salt treatment 6.6 mg/m³ ($n = 14$), high-salt treatment 10.8 mg/m³ ($n = 15$) or placebo 0.3 mg/m³ ($n = 10$) 10 times in a 2 weeks' period in a double-blind manner.

Results: The level of induced sputum eosinophilic cationic protein µg/l, was 3070 before and 4651 after the low-salt treatment period, on average. In the high-salt treatment group, it was 12 192 µg/l vs 11 803 and in the placebo group 3942 vs 4144, respectively. Salt chamber treatment had no effect on sputum eosinophil or neutrophil cell numbers.

Conclusions: The reduction in hyper-responsiveness observed in the previous study is probably not due to the effect on eosinophilic inflammation.

Asthma is characterized by the influx of inflammatory cells, especially eosinophils, into the bronchial mucosa, as well as by variable airflow limitation. However, the association between lung function and the underlying inflammation is not straightforward (1, 2). Eosinophilic cationic protein (ECP) is currently one of the most widely used clinical markers of eosinophil activity in asthma (3). Sputum ECP has been found to be more sensitive marker of airway inflammation and asthma severity than serum ECP (4).

The microclimatic conditions of natural cast caves have been used mostly in Central and Eastern Europe for treating asthma (called speleotherapy). Natural dry sodium chloride dust, which is formed as a result of convection–diffusion from salty walls, has been proposed to be the main microclimatic treatment factor. To simulate the microclimate of salt mines, 'salt chambers' have been constructed and they have been proposed to use for the treatment of many sicknesses, including asthma. We have previously shown that salt chamber treatment reduces airway hyper-responsiveness (AHR) as

an add-on therapy in asthmatics on inhaled corticosteroids (ICS) (5). The aim of this study was to assess whether this effect is due to the suppression of airway inflammation. A parallel-group, double-blind, randomized placebo-controlled trial was conducted.

The patients had given written consent to take part in the follow-up schedule. The study was approved by the Ethics Committee of the Central Hospital of South Karelia.

Material and methods

Female and male asthmatics of mild or moderate severity and at least 18 years old were recruited through a local newspaper advertisement. The study nurse made a telephone interview to 146 respondents, and 39 adult patients (mean age 59 years, 79% women) were included in the study. They fulfilled the inclusion criteria: (1) physician-diagnosed asthma, (2) maintenance treatment with inhaled corticosteroids (ICS with a mean dose 653 µg) at least 1 month prior to the

study, (3) no other chronic respiratory diseases or smoking ≥ 10 pack-years, and (4) no acute infection.

After a 2-week baseline period, the patients were randomized to a 2-week (2×5 days) low-salt treatment (mean salt concentration 6.6 mg/m^3), a high-salt treatment (10.8 mg/m^3), or a placebo treatment (0.3 mg/m^3). Patients continued their original asthma medication throughout the study, and the salt chamber treatment acted as an add-on therapy. The 3 groups did not differ in age, duration of asthma, ICS dose, atopy (skin prick test positivity), or lung volumes (FEV_1 , FVC). All 39 asthmatics completed the study.

The salt chamber was 12.5 m^2 in area with a volume of 27.5 m^3 . The roof, walls, and partly also the floor were covered with 20- to 30-mm-thick coating of salt (rock salt NaCl 98.5%). Both the two active and the placebo treatments were administered in the same salt chamber. During the active treatment, 3 g of salt was fed into the salt generator (Polar and Iris salt generator; Polar Health Oy, Nummela, Finland; IndiumTop LLC, Tallinn, Estonia) at intervals of 5 or 3 min, first being pulverized and then being blown into the chamber through the feed channel. During the placebo treatment, salt was not fed into the salt generator. The generator was, however, running and patients could hear its sound (5).

Induced sputum samples were collected just before the treatments (baseline), immediately after, and 4 weeks after the last treatment. Concentrations of sputum ECP and numbers of eosinophils and neutrophils were measured (6). FEV_1 and FVC were measured before and after the treatments and 4 weeks after the last treatment (Micro Spirometer; Micro Medical Instruments Ltd, Rochester, UK). Daily morning and evening PEF values (mini-Wright peak flow meter; Clement Clark, Harlow, UK), the use of rescue bronchodilator, and asthma symptoms were recorded by the patients in a diary during the 2-week period before the first treatment, through the treatment period, and again 2 weeks prior to the 4-week control visit.

Results

Significant differences in changes between the treatment groups were detected neither in ECP concentrations (Table 1) nor in eosinophil or neutrophil numbers (data not shown). Lung function was not affected by the treatments (Table 2). The use of rescue bronchodilator or asthma symptoms did not differ between the 3 treatment groups (data not shown).

Discussion

As far as we know, there are no double-blind, randomized placebo-controlled studies of the effects of salt chamber on inflammation of asthma before this study. Salt concentrations used for active intervention were based on the treatment practices in Central and Eastern Europe and our previous study (5). Inhalation of higher concentrations of salt might cause bronchoconstriction (7). The patients' asthma was controlled with maintenance ICS, but in 21 patients sputum

Table 1 Induced sputum eosinophilic cationic protein values ($\mu\text{g/l}$) in the 2 salt chamber treatment and placebo groups

	Placebo <i>n</i> = 10		Low salt 6.6 mg/m^3 <i>n</i> = 14		High salt 10.8 mg/m^3 <i>n</i> = 15	
	Mean	SD	Mean	SD	Mean	SD
Before treatment	3942	2829	3070	3502	12192	14853
After 2-week treatment	4144	2093	4651	5028	11803	14971
Four weeks after treatment	5489	4235	6213	6186	8801	12305

Repeated-measures ANOVA. Group $P = 0.2293$, Time $P = 0.9320$, Time*Group $P = 0.1379$.

Table 2 FEV_1 , FVC, morning PEF, and evening PEF in placebo and two salt treatment groups

	Placebo (<i>n</i> = 10)		6.6 mg/m^3 (<i>n</i> = 14)		10.8 mg/m^3 (<i>n</i> = 15)	
	Mean	SD	Mean	SD	Mean	SD
FEV_1						
Baseline	2.37	0.32	2.70	0.57	2.76	0.60
Treatment	2.37	0.34	2.72	0.58	2.71	0.61
Control	2.44	0.53	2.65	0.59	2.88	0.62
FVC						
Baseline	3.35	0.44	3.92	0.99	3.95	0.97
Treatment	3.36	0.55	3.96	0.96	3.84	0.97
Control	3.35	0.53	3.84	1.01	4.03	0.99
PEF morning						
Baseline	409.80	66.59	431.21	50.51	461.93	85.99
Treatment	424.89	67.66	436.50	59.22	466.27	78.18
Control	430.11	67.62	439.23	60.14	480.67	73.70
PEF evening						
Baseline	420.40	70.32	438.57	52.81	471.47	85.15
Treatment	438.56	64.70	445.50	59.55	478.00	79.69
Control	438.56	69.49	443.54	57.09	489.33	78.92

Kruskal-Wallis; FEV_1 Treatment effect $P = 0.353$, Follow effect $P = 0.766$.

FVC Treatment effect $P = 0.555$, Follow effect $P = 0.624$.

PEF morning Treatment effect $P = 0.411$, Follow effect $P = 0.667$.

PEF evening Treatment effect $P = 0.022$, Follow effect $P = 0.855$.

ECP values were higher than the reference of $2500 \mu\text{g/l}$ (8). This indicated room for improvement in anti-inflammatory treatment. However, salt chamber treatment did not affect any of the eosinophilic markers.

AHR is regarded as a major functional abnormality in asthma, reflecting the abnormalities of airway smooth muscle (9). Ventilation heterogeneity changes have been shown to correlate strongly with the changes in AHR independent of inflammation (10). This might be one explanation of the outcome of salt chamber treatment on AHR without any detected anti-inflammatory effects.

So far, there is no evidence of any anti-inflammatory effect of salt chamber treatment on asthmatic airways. The possible effect of the salt chamber treatment on inflammatory markers in pre-asthma or steroid-naïve asthma patients should be investigated in the further studies.

Acknowledgments

The study was supported by research grants from Finland's Slot Machine Association and The Social Insurance Institution of Finland.

References

1. Crimi E, Spanevello A, Neri M, Ind PW, Rossi GA, Brusasco V. Dissociation between airway inflammation and airway hyperresponsiveness in allergic asthma. *Am J Crit Care Med* 1998;**157**:4–9.
2. Kauppinen RS, Vilkkä V, Hedman J, Sintonen H. Ten-year follow-up of early intensive self-management guidance in newly diagnosed patients with asthma. *J Asthma* 2011;**48**:945–951.
3. Venge P. Monitoring the allergic inflammation. *Allergy* 2004;**59**:26–32.
4. Pizzichini E, Pizzichini MM, Efthimiadis A, Dolovich J, Hargreave FE. Measuring airway inflammation in asthma: eosinophils and eosinophilic cationic protein in induced sputum compared with peripheral blood. *J Allergy Clin Immunol* 1997;**99**:539–544.
5. Hedman J, Hugg T, Sandell J, Haahtela T. The effect of salt chamber treatment on bronchial hyperresponsiveness in asthmatics. *Allergy* 2006;**61**:605–610.
6. Djukanovic R, Sterk PJ, Fahy JV, Hargreave FE. Standardised methodology of sputum induction and processing. *Eur Respir J Suppl* 2002;**37**:1s–2s.
7. Anderson SD, Spring J, Moore B, Rodwell LT, Spalding N, Gonda I et al. The effect of inhaling a dry powder of sodium chloride on the airways of asthmatic subjects. *Eur Respir J* 1997;**10**:2465–2473.
8. Metso T, Ryttilä P, Peterson C, Haahtela T. Granulocyte markers in induced sputum in patients with respiratory disorders and healthy persons obtained by two sputum-processing methods. *Respir Med* 2001;**95**:48–55.
9. Zuyderduyn S, Sukkar MB, Fust A, Dhaliwal S, Burgess JK. Treating asthma means treating airway smooth muscle cells. *Eur Respir J* 2008;**32**:265–274.
10. Downie SR, Salome CM, Verbanck S, Thompson B, Berend N, King GG. Ventilation heterogeneity is a major determinant of airway hyperresponsiveness in asthma, independent of airway inflammation. *Thorax* 2007;**62**:684–689.

Authors' contribution

JS involved in clinical examination, data gathering, and analyzing, writing of the manuscript. JH involved in writing of the manuscript and study design. KS involved in data gathering and study design. TH involved in study design and writing of the manuscript, and is a scientific advisor.

Conflict of interest

The authors declare no conflicts of interests.