Determinants of specific sensitization in flour allergens in workers in bakeries with use of skin prick tests

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Abstract. – Baker's asthma, like other forms of occupational asthma is probably the most serious manifestation of occupational allergy among bakery workers. It is caused by immunologic sensitization and subsequent allergic reactions in the airways to occupational specific airborne allergens. Skin Prick Tests (SPTs) play an important role in the diagnosis of baker's asthma and epidemiological field studies on frequencies of sensitization to flour. This paper presents a review of the available literature on prevalence of flours sensitization in bakery workers. Atopy and level of exposure appears to be a very strong determinant for sensitization to flour allergens. Prevention strategies and standard setting are discussed.

Key Words:

Baker's asthma, Skin prick tests, Wheat flour, Specific sensitization, Atopy.

Introduction

Bernardo Ramazzini reported illness associated with baking as early as 1713, including symptoms of cough, shortness of breath, hoarseness, asthma, and eye problems. The primary work related illness associated with flour exposure continues to be rhinitis, conjunctivitis, baker's asthma and dermatitis. The most serious of these is baker's asthma¹.

Baking and biscuit, pastry and cake making processes all involve flour exposures. In small scale bakeries exposure levels have been found to be highest during mixing and baking stages, but in larger bakeries exposures to flour can occur during receipt and opening of flour containers, mixing and baking operations, regardless of the product²⁻⁵.

Although the diseases process leading to the development of baker's asthma is not entirely understood, most evidence indicates that the primary mechanism is a Gell and Coombs type I immunoglobulin E (IgE) immediate hypersensitivity reaction⁶⁻⁹. This reaction generally develops shortly after exposure to the antigen, as evidenced by positive skin tests or serum radioimmunoassay tests. The SPT tests have higher sensitivity and specificity than RAST tests (0.23 and 1.00 v 0.20 and 0.93 respectively)¹⁰.

In many studies (Tables I, II) Authors have tried to reveal the prevalence and the determinants of specific sensitization of bakery allergens in workers in bakeries in different countries. Therefore, in most studies skin prick tests and a panel of known baker allergens, like wheat flour, fungal a-amylase, rye flour, oat flour, rice flour, barley flour, etc. were used. Wheal diameters were recorded 10-20 minutes after the application of the antigen in the forearm of subjects, using in parallel histamine chloride and allergen diluents as positive and negative controls respectively. Based on the distribution of the responses to the positive control, a mean wheal response diameter of at least 2-3 mm was considered a positive. Also in the majority of the studies, atopic status was defined as a positive skin prick test to one or more common allergens (grass pollen, animal dander, house dust mites, etc).

The aim of the present review is to report the prevalence of flour's sensitization in bakery workers, in contrast with control groups, and to investigate the pathogenetic determinant factors as described in different studies. Thus, a systematic review was performed of published manuscripts between 1986 and 2008 using PubMed. The search

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1 18 18 16 24 sliters -1 15 -1	Ref	Type of Country	Study bakery	Control group	Atopy group	Wheat flour (%)	Fungal α-amylase (%)	Soya flour (%)	Rye flour (%)	Oat flour (%)	Mixed flour (%)	Barley flour (%)	Rice flour (%)	(%)
UK $1MB$ $279(88\%)$ bakers employess $$ 40 $$	12	AU	18 Met B	176 (90%) bakers	24 slicers and wrappers	I	15	I		I	I		I	I
It105 B+PS $226(82\%)$ Bakers and parymakers 119 white ecolar workers 23.9 (110 11.9 (110 $$ ($(((((((($	19	UK	1 MB	279 (88%) bakery employees	I	40	I	I	I	I	5	I	I	
Fr $1 \ln B$ $44 (84.6\%)$ $164 \operatorname{uexposed}$ $$ 11 $ -$ <	13	It	105 B+PS	226 (82%) Bakers and pastry makers	119 whit e collar workers	23.9	11.9		I	I	I	21.7	I	
UK $3MB, 3M, 1FP$ $344 (86\%)$ $ 34$ $ 34$ $ 34$ $ 4$ $ -$ <	14	Fr	1 In B	44 (84.6%)	164 unexposed controls ^a	I	11			I	I		I	I
Fin 4B, IM, ICF 153/62/150 66/15/25 ·· 12/6/8<	20	UK	3MB, 3M, 1 FP	344 (86%)	I	34	I	5			I	4	I	I
UK 19 FB $333(99\%)$ $ 34$ 6 16 6 16 7	23	Fin	4 B, 1 M, 1 CF	153/62/150	I	66/15/25						12/6/8		
Cro C1 93 (92%) 65 unexposed ^b <	24	UK	19 PB	383 (99%)	I	34	6	16	9					4
GermB $89+104^{\circ}$ 43 workers not to bakeries $33/62$ $16/47$ $19/24$ $1/11$ $11/37$ 737 737 UK $3LB$, $3FM$, $1PS$ 246 $ 35.36$ 7.6 4.68 7.7 7.6 3.9 UK $3LB$, $3FM$, $1PS$ 246 $ 35.36$ 7.5 4.68 7.7 7.9 7.9 SerbB 100 $ 18$ 15 15 7.7 7.6 7.7 3.9 Ia $2LB$, $3IM$ $186+111^{d}$ $ 33.6/30$ $20/0.2$ 7.7 7.7 7.7 7.7 7.7 Bel $70SB$, $4IB$ 246 251° 29.9 12.4 7.5 7.7 7.7 7.7 7.7 Nor $6B$ 197 $ 29.9$ 4.7 7.7 7.7 7.7 7.7 7.7	15	Cro	CI	93 (92%)	65 unexposed ^b							25.8		
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Ita 2LB, 3 IM 186+111 ^d - 33.6/30 20/0.2 > <t< td=""><td>26</td><td>Serb</td><td>В</td><td>100</td><td>I</td><td>18</td><td>15</td><td></td><td></td><td></td><td></td><td></td><td></td><td></td></t<>	26	Serb	В	100	I	18	15							
Bel 70 SB, 4 IB 246 251° 29.9 12.4 7.5 3.3 Nor 6 B 197 - 29 4 7 1 1 1	27	Ita	2 LB, 3 IM	186+111 ^d	I	33.6/30	20/0.2							
Nor 6 B 197 - 29 4 7 1 1 1	17	Bel	70 SB, 4 IB	246	251°	29.9	12.4	7.5		3.3				
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Table I. Specific sensitization with flour allergens in bakery workers with skin prick tests in cross sectional studies.

References	Country	Study group	Atopy (%)	Wheat flour (%) ^a	α-amylase (%)ª	Wheat flour (%) ^b	A amylase (%) ^b
29	Italy	125 trainee bakers	-	3.2		10	0.1
30	UK	300 Workers ^c	34	4% ^d	5	12	
31	Canada	188 pastry makers	47.5	5.2		9.67	
32	Poland	287 apprentices	18.8	0.7 %		11.2	

Table II. Specific sensitization with flour allergens in bakery workers with skin prick tests in prospective studies.

a: baseline examination, b: end of study, c: workers in 3 large bakeries, 3 mills and 1 flour packing station, d: mixed flour.

terms that have been used included skin prick tests; sensitization in common allergens, and atopy, in bakers the findings concluded cross-sectional and prospective studies (Tables I, II).

Discussion

Bakery workers usually have sensitization in flour allergens, with the higher prevalence being for wheat flour (4-47%), and for fungal α -amylase (4.68-24%). These results are well predictable since almost all bakeries wheat flour is used for bread manufacturing than α -amylase (as baking additives). The main reason for ranging in prevalence of flour's sensitization is that the methods that have been used varied from study to study, since extracts available for bakery allergens are not standardized, and the origin and concentration of the extracts used for skin prick testing were quite different. However, most of the studies suggested that the prevalence of immunologic sensitization was significant higher in bakers compared to the control groups¹¹.

Also few data are available on sensitization to wheat flour and α -amylase in populations without occupational exposure to these agents¹²⁻¹⁷. The prevalence range in that population was between 0.4 to 6%. These studies suggest that there is at least some background level of sensitization in the general population, probably due to an increased propensity to develop IgE-mediated sensitization in individuals with immunologic sensitization to several common allergens, or as a result of cross reactivity to other allergens, i.e. pollens¹⁸.

The findings of studies above are that atopy appears to be a very strong determinant for sensi-

tization to flour allergens, with reported Odds Ratios range from 3.7 to 20.8. Some studies showed that the level of exposure is also an important risk factor for the immunologic sensitization. Musk et al¹⁹ showed that the sensitization to wheat flour was more common among the highly exposed workers compared with the low exposed workers (OR: 3.0). Cullinan et al²⁰ reported that the frequency of sensitization to wheat flour and α -amylase tended to increase with intensity of both dust exposure and wheat allergen exposure. Also Houba et al²¹ found a strong and positive association between the wheat flour allergen exposure and the wheat flour specific sensitization. In an Italian study¹³ sensitization was significantly associated with cigarette smoking (OR: 2.7), and work seniority (OR: 1.03). Age, sex and gender have not been reported to be determinants of sensitization.

In our study²², which had performed in south west of Greece, among 58 bakers in traditional bakeries, with use of skin prick tests, we found the prevalence of sensitization in wheat flour was 17.24%, with atopy to be a determinant factor (OR=8.8, 95% CI: 1.44-68.94). Also in this paper the percentage of control group (cleaners) with specific sensitization in bakery allergens was 2.2%. It was also shown that the smokers in the group of bread producers showed a slightly decreased risk of sensitization in wheat flour (OR=0.17, 95% CI: 0.03-1.06), results which are in agreement with Niewenhuijsen et al, where the risk of sensitization was increased (prevalence ratio – PR: 0.7), but no significant¹².

Based in prospective studies, positive skin tests in occupational allergens is a significant factor for development work related respiratory symptoms, but not positive skin tests (atopy) in common allergens. So the main purpose for the prevention of bakery allergy must be the examination of atopy, the avoidance immunologic sensitization in bakery allergens and the control of intensity exposure in dust flour, which did not examine in that study.

The prevention must be focused in four stages, including the assessing of bakery dust levels and risk, controlling dust levels, wearing protective clothing and equipment and health surveillance for respiratory issues.

The first step is to determine flour dust levels to which workers are exposed, with measurement of airborne dust levels using sampling apparatus and send samples to a suitable laboratory for analysis. When the dust levels are determined, these can be compared with the flour maximum exposure limit (MEL) and short-term exposure limit (STEL) to help determining the risk. The MEL in Greece is 10 mg/m³ and 5 mg/m³ for inspirable and respirable fraction respectively.

Dust levels can be controlled either by making changes to plant and equipment (engineering controls) or by changing working practices. So an improvement to local exhaust ventilation is mandatory in order to extract dust of machines and at processes that emit dust. Also a thorough examination and test of the dust extraction equipment should be carried out at least every 1-year.

Making simple changes to working practices can greatly reduce worker's exposure to flour dust. Such practices must use dredgers or sprinklers to spread dusting flour, avoidance of spillages of flour and where spillages are used, cleaning should be immediately, avoidance of the use of compressed airlines for cleaning, avoidance of raising dust when loading ingredients into mixers and starting up mixers on slow speed until wet and dry ingredients are combined. Finally the use of alternative forms of flour treatment improver, for example pastes, liquids and dust-suppressed powders eliminate or reduce the risk of breathing in the dust.

Protective clothing and equipment included respirators, who should only be worn where other control measures are not reasonably practicable or do not provide adequate control. For workers with no facial hair, disposable masks classified as type FFP3 or half masks with P3 filters should provide sufficient protection for most short- term tasks (for the prevention from particles). Powdered respirators with P3 filters should be worn by people with facial hair (including those who are unshaven) and for longer-term tasks. Health surveillance must be undertaken to enquire positively about the early symptoms of ill health. At least the following arrangements should be in place:

- Pre-employment screening that includes a questionnaire about present or past asthma or chest illness.
- A questionnaire must be completed by all workers at least annually to enquire about any developing symptoms.
- Skin prick tests at the beginning of working as a baker, for the searching of atopy and then at least annual for the searching of immunologic sensitization in flour allergens.

A major part in the prevention of baker's allergy, either respiratory or immunologic is the involvement and cooperation of an occupational hygiene consultant and a specialist of occupational medicine, who will inform the employers for the hazards of their work, train them, and control the conditions of work. However, in Greece the law commits only the companies with more than 50 workers to use specialist in occupational medicine, as a result no one check the conditions of health and safety in traditional bakeries, where the workers are less from 5. So the solution may be the contact of federation of bakers with specialist in occupational medicine for the major of bakers, and no for each bakery separately.

References

- RAMAZZINI B. Diseases of workers. The University of Chicago Press, Chicago, 1940.
- BURDORF A, LILLIENBERG L, BRISMEN J. Characterization of exposure to inhalable flour dust in Swedish bakeries. Ann Occup Hyg 1994; 38: 67-78.
- JAUHIAINEN A, LOUHELAININ K, KINNAINMAA M. Exposure to dust and alpha-amylase in bakeries. Appl Occup Environ Hyg 1993; 8: 721-725.
- NIEUWENHUIJSEN MJ, SANDIFORD CP, LOWSON D, TEE RD, VENABLES KM, McDONALD JC, NEWMAN TAYLOR AJ. Dust and flour aeroallergen exposure in flour mills and bakeries. Occup Environ Med 1994; 51: 584-588.
- NIEUWENHUIJSEN MJ, SANDIFORD CP, LOWSON D, TEE RD, VENABLES KM, NEWMAN TAYLOR AJ. Peak exposure concentrations of dust and flour aeroallergen in flour mills and bakeries. Ann Occup Hyg 1995; 39: 193-201.

- 6) CHANG-YEUNG M. Occupational asthma. Chest 1990; 98: 148-161.
- ZEITZ H. Baker's asthma. Allergy Proc 1990; 11: 63-64.
- WILBUR RD, WARD GW. Immunologic studies in a case of a baker's asthma. J Allergy Clin Immunol 1976; 58: 366-372.
- FRANKEN J, STAPHAN U, MEYER HE, KONIG W. Identification of alpha amylase inhibiter as a major allergen of wheat flour. Int Arch Allergy Immunol 1994; 104: 171-174.
- MAJAMAA H, MOISIO P, HOLM K, TURJANMAA K. Wheat allergy:diagnostic accuracy of skin prick and patch tests and specific IgE. Allergy 1999, 54, 851-856
- 11) HOUBA R, DOEKES G, HEEDERIK D. Occupational respiratory allergy in bakery workers: a review of the literature. Am J Ind Med 1998; 34: 529-546.
- PRICHARD MG, RYAN G, MUSK AW. Wheat flour sensitization and airways disease in urban bakers. Br J Ind Med 1984; 41: 450-454.
- DE ZOTTI R, LARESE F, BOVENZI M, NEGRO C, MOLINARI S. Allergic airway in Italian bakers and pastry makers. Occup Environ Med 1994; 51: 548-552.
- 14) BOHADANA AB, MASSIN N, WILD P, KOLOPP M-N, TOA-MAIN J-P. Respiratory symptoms and airway responsiveness in apparently healthy workers exposed to flour dust. Eur Respir J 1994; 7: 1070-1076.
- 15) ZUSKIN E, KANCELIAK B, SCHACHTER EN, GODNIC-CVAR J, MUSTAJBEGOVIC J, BUDAK A. Respiratory function and immunological status in cocoa and flour processing workers. Am J Ind Med 1998; 33: 24-32.
- BAUR X, DEGENS P, SANDER I. Baker's asthma: still among the most frequent occupational respiratory disorders. Allergy Clin Immunol 1998; 102: 984-997.
- 17) DROSTE J, MYNY K, VAN SPRUNDEL M, KUSTERS E, BULAT P, BRAECKMAN L, VERMEIRE P, VANHOORNE M. Allergic sensitization, symptoms, and lung function among bakery workers as compared with a nonexposed work population. J Occup Environ Med 2003; 45: 648-655.
- 18) GAUTRIN D, INFANTE-RIVARD C, DAO TV, MAGNAN-LAROSE M, DESJARDINS D, MALO JM. Specific IgE-dependent Sensitization, atopy, and bronchial hyperresponsiveness in apprentices starting exposure to protein derived agents. Am J Respir Crit Care Med 1997; 155:1841-1847
- MUSK AW, VENABLES KM, CROOK B, et al. Respiratory symptoms, lung function, and sensitization to flour in a British bakery. Br J Ind Med 1989; 46: 636-642.
- 20) Cullinan P, Lowson D, Nieuwenhuijsen MJ, Sandiford C, Tee RD, Venables KM, McDonald JC, New-

MAN TAYLOR AJ. Work related symptoms, sensitization, and estimated exposure in workers not previously exposed to flour. Occup Environ Med 1994; 51: 579-583.

- HOUBA R, HEEDERIK D, DOEKES G. Wheat sensitization and work related symptoms in the baking industry are preventable. Am J Respir Crit Care Med 1998; 158: 1499-1503.
- 22) KARKOULIAS K, PATOUCHAS D, ALAHIOTIS S, TSIAMITA M, VRODAKIS K, SPIROPOULOS K. Specific sensitization in wheat flour and contributing factors in traditional bakers. Eur Rev Med Pharmacol Sci 2007; 11: 141-148.
- VANHANEN M, TUOMI T, HOKKANEN H, TUPASELA O, TUOMAINEN A, HOLMBERG PC, LEISOLA M, NORDMAN H. Enzyme exposure and enzyme sensitization in the baking industry. Occup Environ Med 1996; 53: 670-676.
- SMITH TA, LUMLEY KPS, HUI EHK. Allergy in flour and fungal amylase in bakery workers. Occup Med 1997; 47: 21-24.
- 25) NIEUWENHUIJSEN MJ, HEEDERIK D, DOEKES G, VENABLES KM, NEWMAN TAYLOR AJ. Exposure-response relations of a amylase sensitization in British bakeries and flourmills. Occup Environ Med 1999; 56: 197-201.
- 26) PAVLOVIC M, SPASOJEVIC M, TASIC Z, TACEVIC S. Bronchial hyperactivity in bakers and its relation to atopy and skin reactivity. Sci Tot Environ 2001; 270: 71-75.
- 27) TALINI D, BENVENUTI A, CARRARA M, VAGHETTI E, BIANCHI MARTINI L, PAGGIARO PL. Diagnosis of flour induced occupational asthma in a cross sectional study. Respir Med 2002; 96: 236-243.
- 28) STORAAS T, STEINSVÅG SK, FLORVAAG E, IRGENS A, AASEN TB. Occupational rhinitis: diagnostic criteria, relation to lower airway symptoms and IgE sensitization in bakery workers. Acta Otolaryngol 2005; 125: 1211-1217.
- 29) DE ZOTTI R, BOVENZI M. Prospective study of work related respiratory symptoms in trainee bakers. Occup Environ Med 2000; 57: 58-61.
- 30) CULLINAN P, COOK A, NIEUWENHUIJSEN MJ, SANDIFORD C, TEE RD, VENABLES KM, McDONALD JC, NEWMAN TAYLOR AJ. Allergen and dust exposure as determinants of work-related symptoms and sensitization in a cohort of flour-exposed workers; a case-control analysis. Ann Occup Hyg 2001; 45: 97-103.
- GAUTRIN D, GHEZZO H, INFANTE-RIVARD C, MALO JL. Incidence and host determinants of work related rhinoconjunctivitis in apprentice pastry-makers. Allergy 2002; 57: 913-918.
- 32) WALLUSIAK J, HANKE W, GORSKI P, PATCZYNSKI C. Respiratory allergy in apperentice bakers: do occupational allergies follow the allergic march? Allergy 2004; 59: 442-4502.