

Changing patterns of contact allergy in chronic inflammatory ear disease

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Chronic inflammatory ear disease comprises a wide range of conditions. Although contact allergy to topical medicaments is common in such conditions, the causes of these reactions have not been examined in a large series for over a decade. Our aim was to investigate the major sensitizers recorded in 179 patients over the last 17 years. Medicament contact allergic dermatitis was diagnosed in 45 patients (25%), of whom 34 (76%) demonstrated a relevant allergy to neomycin, 28 (62%) to framycetin, 11 (31%) to gentamicin, 8 (18%) to quinoline mix and 5 (11%) to caine mix. Of all neomycin-allergic patients, 28 (76%) were also allergic to framycetin and 12 (43%) to gentamicin. Comparing the first 60 patients (1985–94) to the most recent 60 (1998–2002) identified a significant recent reduction in the number of patients allergic to neomycin ($P=0.002$) and framycetin ($P=0.050$), with a non-significant reduction in the total number diagnosed as medicament-allergic ($P=0.066$). We have therefore demonstrated a high frequency of medicament contact allergy in chronic inflammatory ear disease, supporting the routine use of patch testing in these patients. We have also shown a significant recent reduction in the number of such patients with allergy to neomycin and framycetin.

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Chronic inflammatory ear disease comprises a range of conditions, including idiopathic otitis externa, seborrhoeic dermatitis, atopic dermatitis, contact dermatitis and psoriasis. A variety of topical medicaments are available, and although contact allergy to medicaments is common in such conditions, the causes of these reactions have not been examined in a large series for over a decade. Earlier studies identified the aminoglycoside antibiotics neomycin, framycetin and gentamicin as the most frequent sensitizers, and almost universally recommended avoidance of routine or prolonged use (1–3).

The aim of this study was therefore to examine the major sensitizers recorded in a large series of patients over the last two decades, and to identify any trends in contact allergy, particularly to the aminoglycosides, during that period.

Patients and Methods

Patients

Patch testing records were reviewed on consecutive patients presenting with chronic inflammatory ear disease between 1985 and 2002. All patients were patch tested to the departmental standard series, in

addition to a departmental ear medicament series (Table 1). Gentamicin was used routinely in the ear series only on the 149 patients tested since 1990. Patch tests were performed according to International Contact Dermatitis Research Group (ICDRG) recommendations (4).

Data collection

Demographic data including age, sex and ethnic origin were recorded, in addition to the referring department, duration of symptoms and presence or absence of atopic eczema, asthma or hay fever. Positive patch tests were recorded and, only if clinically relevant, a diagnosis of medicament contact allergy made.

The frequency of contact allergy to individual sensitizers was compared between the first third and the last third of the study population using standard 2 by 2 chi-square tests (χ^2).

Results

Demographics

The study population comprised 179 patients with chronic inflammatory ear disease, including

Table 1. Departmental ear series

Number	Allergen	Concentration (%)
1	Phenazone	10
2	Tetracycline	02
3	Nitrofurazone	01
4	Bacitracin	20
5	Gramicidin	10
6	Nystatin	10
7	Polymyxin B sulphate	03
8	Sulfacetamide	05
9	Gentamicin	20
10	Chloramphenicol	05
11	Framycetin sulphate	20
12	Polyethylene glycol 400	30
13	Pot hydroxyquinoline sulphate	01
14	Bismuth subnitrate	10
15	Iodoform	10

54 males (30%) and 125 females (70%). 176 were Caucasian (98%). The mean age in males was 55 years (range 4–84) and in females was 45 years (range 8–94). Mean age was not influenced by the presence or absence of medicament-allergy (48 years in both groups).

Referring department

Data were recorded on 152 patients, of whom 121 (80%) were referred for patch testing from the dermatology department, 29 (19%) from the ear, nose and throat (ENT) department and 2 (1%) direct from general practice.

Symptom duration

The median duration of symptoms was 48 months, shorter in males (36 months) than in females (48 months). Atopics had a longer duration of symptoms (54 months) than non-atopics (38 months). The presence or absence of medicament allergy made no difference to the median duration of symptoms (48 months in both groups).

Patch test results

Positive patch test reactions to allergens in the departmental ear series were recorded in 34 individuals (19%) with 29 to framycetin and 12 to gentamicin and relatively few reactions to non-aminoglycosides (Table 2). 37 (21%) had positive patch test reactions to neomycin (in the standard series), which was even more common than nickel allergy (30 patients, 17%). Medicament contact allergic dermatitis was diagnosed in 45 patients (25%), of whom 34 (76%) demonstrated a relevant allergy to neomycin, 28 (62%) to framycetin, 11 (31% of 149 patients after 1989) to gentamicin, 8 (18%) to quinoline mix and 5 (11%) to caine

Table 2. Number of positive patch test reactions to the departmental ear series. Figures in brackets are the percentage of all 179 patients

Allergen	Number of positive reactions
Framycetin	29 (16%)
Gentamicin	12 (8%)
Iodoform	3 (2%)
Gramicidin	1 (1%)
Paradichlorobenzene	1
Polyethylene glycol 400	1
Terpentine	1
Potassium hydroxyquinoline sulphate	1

mix (Table 3). A positive patch test was not considered 'relevant' if there was no corresponding history of medicament application to the ear.

Of the 37 neomycin-allergic patients, 28 (76%) were also allergic to framycetin and 12 (43% of 28 patients after 1989) to gentamicin. Of the framycetin and gentamicin allergic patients (41 in total), all but 1 were neomycin-allergic, demonstrating very strong co-reactivity amongst the aminoglycosides.

Table 3. Relevant sensitizers when medicament contact allergy was diagnosed. Figures in brackets are the percentage of all 45 patients with medicament contact allergy

Allergen	Number
Departmental ear series	
Framycetin	28 (62%)
Gentamicin	11 (31%)
Iodoform	3 (7%)
Gramicidin	1 (2%)
Paradichlorobenzene	1
Polyethylene glycol 400	1
Terpentine	1
Potassium hydroxyquinoline sulphate	1
Departmental standard series	
Neomycin	34 (76%)
Quinoline mix	8 (18%)
(Nickel)	7
Caine mix	5 (11%)
Wood tars	3 (7%)
Ethylenediaminetetraacetic acid	3 (7%)
Tixocortol pivalate	2 (4%)
Colophonium	2 (4%)
(Fragrance mix)	2
(Cobalt)	1
Budesonide	1 (2%)
Myroxylon pereirae resin	1
(Mercaptobenzoethiazole)	1
(Mercapto mix)	1
Lanolin alcohol	1
Amerchol L101	1
Methylchloroisothiazolinone +	1
Methylisothiazolinone	

Non-medicament allergens are in brackets. Percentages refer to the percentage of medicament-allergic patients (45).

Table 4. Comparison of the first and last 60 patients in the study

	Medicament-allergic contact dermatitis	Neomycin allergy	Framycetin allergy
First 60 (1985 to 94)	21	20	14
Last 60 (1998 to 2002)	12	6	6
Chi-square	3.39	9.62	3.84
<i>P</i>	0.066	0.002	0.050

Only 14, 11 and 17% of allergic reactions to neomycin, framycetin and gentamicin, respectively, were detected at the 2-day reading, increasing to 92, 79 and 83%, respectively, by 4 days. However, a respective 8, 21 and 17% were delayed, developing the first signs of an allergic reaction after the 4-day reading.

Comparing the first 60 patients in the study (1985–94) to the most recent 60 (1998–2002) identified a significant recent reduction in the number of patients allergic to neomycin ($P=0.002$) and framycetin ($P=0.050$), with a non-significant reduction in the total number diagnosed as medicament-allergic ($P=0.066$) (Table 4). There was no overall difference between the two groups in the total number diagnosed as allergic contact dermatitis ($P=0.73$), which suggests that the observed trends are real.

65 individuals (36%) gave a personal history of atopy. 20 of the atopics (31%) were subsequently found to be medicament-allergic, compared to 25 of 114 non-atopics (22%).

Discussion

In a large series of consecutive patients with chronic inflammatory ear disease over the last 17 years, we have demonstrated a high frequency of medicament contact allergy, supporting the routine use of patch testing in the management of these conditions. We have also shown a significant recent reduction in the number of such patients found to be allergic to neomycin and framycetin. We have demonstrated strong co-reactivity amongst the aminoglycosides, and

confirmed that a significant proportion of patients allergic to aminoglycosides (up to 21%) will be missed if not followed up after the 4-day reading.

Contact allergy to the aminoglycosides in chronic inflammatory ear disease has been well reported throughout the last 3 decades, with most authors recommending avoidance of routine or prolonged use in such conditions. Kirton and Munro-Ashman (5) and Jensen et al. (6) brought the problem to the attention of general physicians. The overall percentages of patients with allergic patch test reactions in our series to neomycin (21%), framycetin (16%) and gentamicin (8%) are similar to the mean figures from previous studies (Table 5), emphasizing that the trends are found within our sample, not by comparing it to other samples in other countries. The significant reduction in neomycin and framycetin contact allergy over the last 2 decades probably reflects acknowledgement of these reports, and consequently more careful prescribing by general practitioners, ENT surgeons and dermatologists.

Comparing our demographic data to that of previous studies, our observed female predominance in patients with chronic inflammatory ear disease attending for patch testing (125 females versus 54 males) is consistent with 2 previous studies that reported a sex ratio (2, 6). However, our observation of the same mean age in those with and without medicament contact allergy (48 years) contrasts with that of Smith et al. (2), who found that their patients with chronic otitis externa and contact allergy (57 years) were older than those without contact allergy (35 years); they suggested that contact allergy 'is not an

Table 5. Previous studies of positive allergic patch tests to aminoglycosides in chronic ear disease

Author	Year	Total number	Neomycin (%)	Framycetin (%)	Gentamicin (%)
Rasmussen (8)	1974	98	8	ND	ND
Holmes et al. (1)	1982	40	15	15	10
Fraki et al. (9)	1985	142	16	16	1
Smith et al. (2)	1990	37	32	27	5
Onder et al. (7)	1994	40	35	ND	23
Van Ginkel et al. (3)	1995	34	35	35	26
Mean (%)			24	16	18

ND, no data.

aetiological factor in the younger patient' with otitis externa, a conclusion that our study does not support. The 48-month median duration of symptoms in our study was the same in those with and without medicament contact allergy, a finding also observed by Smith et al. and which suggests that the presence of a relevant contact allergen usually goes unnoticed by the patient or prescribing physician.

In summary, we have therefore demonstrated a high prevalence of medicament contact allergy in chronic inflammatory ear disease, supporting the routine use of patch testing in these patients. We have also shown a significant recent reduction in the number of such patients allergic to neomycin and framycetin.

References

1. Holmes R C, Johns A N, Wilkinson J D, Black M M. Medicament contact dermatitis in patients with chronic inflammatory ear disease. *J R Soc Med* 1982; 75: 27-30.
2. Smith I M, Keay D G, Buxton P K. Contact hypersensitivity in patients with chronic otitis externa. *Clin Otolaryngol* 1990; 15: 155-158.

3. Van Ginkel C J W, Bruintjes T D, Huizing E H. Allergy due to topical medications in chronic otitis externa and chronic otitis media. *Clin Otolaryngol* 1995; 20: 326-328.
4. Fregert S. *Manual of Contact Dermatitis*, 2nd edn. Copenhagen: Munksgaard, 1981: 71-81.
5. Kirton V, Munro-Ashman D. Contact dermatitis from neomycin and framycetin. *The Lancet* 1965: 138-139.
6. Jensen O C, Allen H J, Mordecai L R. Neomycin contact dermatitis superimposed on otitis externa. *JAMA* 1966: 195: 175-177.
7. Onder M, Onder T, Ozunlu A, Seyed Makki S, Ali Gurer M. An investigation of contact dermatitis in patients with chronic otitis externa. *Contact Dermatitis* 1994; 31: 116-134.
8. Rasmussen P A. Otitis externa and allergic contact dermatitis. *Acta Otolaryngol* 1974; 77: 344-347.
9. Fraki J E, Kalimo K, Tuohimaa P, Aantaa E. Contact allergy to various components of topical preparations for treatment of external otitis. *Acta Otolaryngol (Stockh)* 1985; 100: 414-418.

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