

Royal jelly consumption and hypersensitivity in the community

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Summary

Background Royal jelly consumption has recently been linked with acute asthma, anaphylaxis and death. A cross-sectional survey was conducted to determine the prevalence of and the relationship between royal jelly consumption and hypersensitivity reactions.

Methods 1472 hospital employees of a teaching hospital in Hong Kong completed a questionnaire on royal jelly consumption and related allergic symptoms, and 176 questionnaire respondents and 300 consecutive asthma clinic patients were skin tested to royal jelly.

Results Royal jelly consumption was high, with 461 out of 1472 subjects (31.3%) having taken royal jelly in the past. A total of nine subjects reported 14 adverse reactions to royal jelly, including urticaria, eczema, rhinitis and acute asthma. Thirteen out of 176 questionnaire respondents (7.4%) and 23 out of 300 consecutive asthma clinic attendees (7.3%) had positive skin test to pure royal jelly. All but one of the 36 subjects with positive royal jelly skin test were atopic to other common allergens. Positive associations were found between positive royal jelly skin test and atopy (OR = 33.73, 95% CI 4.51 to 252.11), adverse reactions to royal jelly and a history of clinical allergy (OR = 2.88, 95% CI 0.72 to 11.58), but not between royal jelly symptoms and previous royal jelly intake.

Conclusion Royal jelly consumption is high in the community of Hong Kong. Atopic individuals are at high risk of sensitization to royal jelly but the precise relationship between royal jelly use, positive royal jelly skin test and clinical manifestations of adverse reactions to royal jelly, remains to be defined.

Keywords: royal jelly, allergy, asthma, eczema, rhinitis, anaphylaxis, food hypersensitivity, atopy, skin test, epidemiology, Chinese

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Introduction

Royal jelly is a health tonic widely consumed in the community, with perceived benefits ranging from promotion of growth in children and improvement of general health status to enhancement of longevity for the elderly. Since the two reports of adverse reactions to royal jelly, including a death from acute asthma, in Australia in 1993 [1,2], the Therapeutics Goods Authority and National Food Authority in Australia issued a warning to caution the intake of preparations containing royal jelly in asthma and allergy

suffers. The first case of royal jelly-induced asthma in the United Kingdom was recently reported [3], and royal jelly was also implicated in the death of a young asthmatic woman who developed acute bronchospasm and lost consciousness shortly after taking royal jelly capsules, ironically for her asthma (F. Thien, personal communication).

All the reported cases of royal jelly allergy to date occurred in atopic subjects with clinical allergy. A number of royal jelly proteins, with molecular weights ranging from 47 to 55kD, which are thought to be allergenic have recently been identified [4]. However, the presence of IgE binding to these proteins is not specific for clinical royal jelly allergy and is also found in subjects with allergic manifestations other than royal jelly hypersensitivity, suggesting possible

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cross-reactivity between royal jelly proteins and other common environmental allergens. There have not been any reports of adverse reactions to royal jelly in Chinese populations where the consumption of royal jelly as a health tonic originated. Whether this is due to a lack of awareness or relative resistance to royal jelly hypersensitivity amongst Chinese people is uncertain. In this paper, we determined the prevalence of royal jelly hypersensitivity and its relationship with royal jelly use in Hong Kong.

Methods

Written questionnaires were sent to all 2000 hospital employees of the Prince of Wales Hospital for completion. There were questions on the frequency of and indications for royal jelly use, adverse reactions associated with royal jelly, and personal history of clinical allergy. The questionnaire respondents were asked to undergo skin prick testing to royal jelly and common inhalant allergens at a later date. A further 300 consecutive asthma clinic attendees were also skin tested, and those with positive skin tests to royal jelly completed the same questionnaire and the results were analysed together with the hospital sample.

Fresh royal jelly (preservative free) was obtained directly from the Beijing Dietetic Preparation Manufactory which is a major manufacturer of royal jelly products in Beijing and an exporter of raw royal jelly to other countries for local processing. The raw royal jelly was applied directly on the forearm without addition of diluents in skin testing. Other allergen extracts used in skin testing were house dust mite (*D. pteronyssinus*, *D. farinae*), cockroach mix (American, German, Oriental spp.), *Alternaria*, *Aspergillus*, *Cladosporium*, *Penicillium*, cat hair, Bermuda grass (*C. dactylon*), and ragweed pollen (Hollister-Stier, Spokane, Washington).

Skin tests were performed according to Pepys' method [5] using histamine (10 mg/ml) and normal saline as positive and negative controls respectively. If a reaction occurred after 15 min, the transverse and vertical diameter of the wheal was measured and mean values recorded. Wheals of 3 mm or greater were regarded as positive in the absence of a reaction to normal saline. Atopy is defined as one or more positive skin tests to the common environmental allergens.

Data were categorized and analysed using SPSS for Windows [6]. The χ^2 test was used to assess the association between categorical variables. The Mann-Whitney test was used to determine the association between the wheal size of positive royal jelly skin test and adverse reactions to royal jelly, and between royal jelly usage and wheal size of positive royal jelly skin test. Estimates of odds ratios, standard errors and confidence intervals were based

on asymptomatic likelihood theory. A significance level of $P < 0.05$ was used.

Results

Out of the 2000 questionnaires sent, 1472 were returned completed, representing a response rate of 73.6%. Table 1 shows the questionnaire response. A total of 461 subjects (31.3%) admitted taking royal jelly in the past, usually in the form of ampoules (86.5%). Whilst 62% took royal jelly to improve general health status, up to 20% were unsure of its benefits. Of the 461 subjects who had taken royal jelly before, 128 or 27.8% had done so in the 12 months prior to the survey with an average consumption of 3.7 ampoules (range 1 to 40) or 17 capsules (range 1 to 100) in the past year.

A total of nine subjects (0.6%) reported 13 adverse reactions to royal jelly and these included urticaria, eczema, conjunctivitis, rhinitis and dyspnoea. One asthmatic patient developed a mild asthma exacerbation which was promptly controlled with inhaled salbutamol. Two patients had more than one allergic reaction occurring within 2 h of taking royal jelly. Two-thirds gave a history of allergic disease in the past. There was an association between adverse reactions to royal jelly and a history of clinical allergy, although it did not reach statistical significance (odds ratio = 2.88, 95% CI 0.72 to 11.58).

One hundred and seventy-six subjects, including six of the nine subjects with alleged royal jelly reactions, underwent skin testing and the results are shown in Table 2. Thirteen subjects (7.4%) reacted positively to pure royal jelly with wheal sizes ranging from 3 to 7 mm. Only three of the 13 subjects (23.1%) with positive skin test to royal jelly had taken royal jelly in the past. No correlation between royal jelly skin test and royal jelly-induced symptoms can be found ($P = 0.38$). Of the 300 consecutive skin tests performed in the asthma clinic, 23 had positive skin test to royal jelly, representing a prevalence of 7.7%. Of these 23 subjects, 10 (29.4%) reported taking royal jelly in the past but none recalled any associated adverse reactions.

When the skin test and questionnaire data of the 36 positive skin test responders to royal jelly were combined, there did not appear to be any association between skin test positivity to royal jelly and a history of royal jelly use (odds ratio = 0.65, 95% CI 0.29 to 1.45). The wheal size of the positive royal jelly skin tests was not related to a history of adverse reactions to royal jelly or a history of clinical allergy. In contrast, 35 of 36 subjects (97.2%) with positive skin test to royal jelly were atopic to other common allergens, indicating a significant association between atopic status and positive skin test to royal jelly (odds ratio = 33.73, 95% CI 4.50 to 252.11).

Table 1. Questionnaire response

	Number	%	95% confidence intervals
Response rate	1472	73.6	
Age (yr)			
< 20	71	4.8	
20–30	797	54.1	
31–40	452	30.7	
> 40	152	10.3	
Sex			
Female	1132	79.6	
Male	340	24.1	
History of allergic disease			
Allergic rhinitis	414	28.1	25.8–40.4
Eczema	307	20.9	18.8–22.9
Asthma	61	4.1	3.1–5.2
≥ 1 of above	605	41.1	38.6–43.6
Royal jelly use ever	461	31.3	28.9–33.7
Forms of royal jelly used			
Ampoules	399	27.1	24.8–29.4
Capsules	67	4.6	3.5–5.6
Frequency			
≥ 12 ampoules/yr	5	0.3	0.1–0.8
≥ 12 capsule/yr	10	0.7	0.3–1.1
Adverse reactions to royal jelly	9	0.6	0.2–1.0
Pruritus	2	0.1	0.0–0.5
Urticaria	2	0.1	0.0–0.5
Eczema	2	0.1	0.0–0.5
Conjunctivitis	2	0.1	0.0–0.5
Rhinorrhoea	2	0.1	0.0–0.5
Dyspnoea	2	0.1	0.0–0.5
Asthma	1	0.1	0.0–0.4

Discussion

We have found a high prevalence of royal jelly consumption of over 30% in our population of hospital employees. Although many of these subjects believed that royal jelly could improve health status and even cure specific diseases, there remains a substantial number who are unsure of its claimed benefits but yet had taken royal jelly preparations, presumably due to the influence of friends and relatives or indirectly through various advertisements in the media. Our sample was biased towards young female health professionals and the prevalence rate for royal jelly use may not be representative of the community of Hong Kong. However, royal jelly is often marketed as remedies to improve school performance for the young, to assist recovery after physical illnesses, and to maintain longevity for the elderly. It will not be surprising to find an even

higher prevalence of royal jelly consumption in these groups of subjects in the community. In fact, a recent study showed that a third of the English-speaking population in the United States used alternative therapy and the prevalence in the non-English speaking populations was estimated to be even higher [7].

The study suffers from inherent recall bias associated with retrospective questionnaire surveys. Nevertheless, the reported adverse reactions with royal jelly were consistent with previous documentations of allergic reactions due to royal jelly ingestion [1]. As some of these adverse reactions occurred many years prior to our study, royal jelly-specific IgE may have fallen to a very low level that could explain the negative royal jelly skin tests in those subjects with previous adverse reactions. Similarly, the lack of association between royal jelly intake and adverse reactions due to royal jelly could be partly due to recall bias, particularly

Table 2. Skin test response in questionnaire respondents

	Number	%	95% confidence intervals
Total	176		
Royal jelly	13	7.4	3.5–11.3
Environmental allergens			
<i>D. pteronyssinus</i>	78	44.3	37.0–51.7
<i>D. farinae</i>	52	29.5	22.8–36.3
Cockroach mix	44	25.0	18.6–31.4
Cat dander	12	6.8	3.1–10.5
<i>Cladosporium</i>	10	5.7	2.3–9.1
<i>Penicillium</i>	4	2.3	0.7–6.1
<i>Aspergillus</i>	1	0.6	0.0–3.6
Bermuda	17	9.7	5.3–14.0
Ragweed	1	0.6	0.0–3.6
Atopy (≥ 1 of above)	95	54.0	46.6–61.3

when royal jelly intake was infrequent and occurred many years earlier and if the reactions were mild.

We found that nearly all our Chinese subjects with positive skin test to royal jelly were atopic and 37.1% had a history of clinical allergy. Leung *et al.* found that specific IgE to the major allergenic proteins in royal jelly was present in up to 38% of Caucasian subjects with clinical allergy but negative royal jelly skin test and no allergic reactions to royal jelly [4]. These observations could suggest possible cross-reactivity between royal jelly proteins and other undefined but ubiquitously distributed environmental allergens, and that atopic individuals become sensitized to royal jelly protein because of molecular mimicry. Alternatively, consumption of royal jelly is so widespread in our community that a considerable proportion of atopic individuals have had previous exposure and become sensitized. However, there remains considerable uncertainty as to whether prior royal jelly usage is a risk factor for sensitization to royal jelly proteins, and whether sensitization is a prerequisite for allergic manifestations upon subsequent exposure. It would be interesting to determine the prevalence of royal jelly consumption and skin test positivity to royal jelly in a Caucasian population to see if a similar relationship between exposure, sensitization and allergic manifestations exists as in our Chinese community.

We also found that subjects with adverse reactions to royal jelly were more likely to have other clinical allergic manifestations. Although the significance of this observation was limited by the relatively small number of royal

jelly-allergic subjects in our study, those with clinical allergy should be cautioned against taking royal jelly supplements.

The royal jelly extract used in our study was obtained from a major manufacturer of royal jelly products from Beijing who assured the investigators that it contained pure royal jelly and was free of any preservatives or additives. The major allergenic components of royal jelly have been identified [4] and allergic reactions to royal jelly products are now considered an IgE-mediated hypersensitivity to a number of royal jelly proteins rather than adverse reactions to preservatives or impurities associated with its processing.

We found a high prevalence of royal jelly consumption in our subject population. Atopy is significantly associated with positive skin test to royal jelly irrespective of previous royal jelly intake and adverse reactions. Further studies should be directed to sequencing and cloning of the major allergenic proteins of royal jelly, and to defining the relationship between exposure, sensitization and allergic manifestations to royal jelly by controlled challenge test and epidemiological research. As all the reported cases of major allergic reactions to royal jelly to date occurred in atopic subjects, indiscriminate use of royal jelly products by these individuals should be discouraged until convincing data suggest otherwise.

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References

- 1 Thien FCK, Leung R, Plomley R, Weiner J, Czarny D. Royal jelly-induced asthma. *Med J Aust* 1993; 159:639.
- 2 Bullock RJ, Rohan A, Straatmans J-A. Fatal royal jelly-induced asthma. *Med J Aust* 1994; 160:44.
- 3 Peacock S, Murray V, Turton C. Respiratory distress and royal jelly. *Br Med J* 1995; 311:1472.
- 4 Thien FCK, Leung R, Baldo B et al. Asthma and anaphylaxis induced by royal jelly. *Clin Exp Allergy* 1996; 26:216–2.
- 5 Pepys J. Skin tests in diagnosis. In: Gell PGH, Coombs PPA, Lachmann PJ, eds. *Clinical aspects of immunology*, 3rd edn. Oxford: Blackwell Science, 1975:55–80.
- 6 SPSS for Windows Release 6.0. Maija J Norusis/SPSS Inc., 1993.
- 7 Eissenberg DM, Kessler RC, Foster C et al. Unconventional medicine in the United States — prevalence, costs, and patterns of use. *N Engl J Med* 1993; 328:246–52.